PHYSICAL ACTIVITY MONITORING IN COPD PATIENTS

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BY

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DECLARATION

This thesis is the result of my own work and was carried out at University Hospital Aintree, Liverpool, UK.

Some of the patient assessments were carried out in part by a physiotherapist or research doctor under my supervision.

The material contained in the thesis has not been presented, nor is currently being presented, either wholly or in part, for any other degree or other qualification.

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ABSTRACT

The importance of physical activity in health and disease is recognised, and its relevance in COPD is of increasing interest since it is related to patient outcomes. This thesis primarily sets out to examine physical activity levels in COPD patients in three clinical situations: The early stages of recovery and the subsequent 4 months after hospitalisation for exacerbation (a prospective cohort study of 60 patients), after a course of pulmonary rehabilitation and 6 months later (a prospective cohort study of 37 patients) and at a stage of disease where long term oxygen therapy is being considered (a retrospective cohort study of 35 patients). We have measured physical activity levels using two types of accelerometer: the DynaPort and the Actiwatch. We have also made measures of lung physiology, exercise capacity, peripheral muscle strength and health status.

COPD patients have very low levels of physical activity when stable, worse still while in hospital recovering from an exacerbation. Across the 3 patient groups, levels of physical activity do not consistently correlate with other measures, suggesting that what patients actually do does not correlate with what they can do or say they can do.

Exacerbating patients who receive early discharge have higher levels of physical activity than those who remain in hospital, and baseline physical activity predicts re exacerbation and readmission at 4 months but not 12 months.

Improvements in levels of physical activity are lost 6 months after completing pulmonary rehabilitation despite preservation of peripheral muscle strength and exercise capacity, suggesting that methods to sustain the benefits of PR should focus on changing patient behaviour rather than simply improving physiology.

COPD patients who use LTOT show comparable levels of physical activity to a similar patient group with better $FEV1_1$ % predicted who do not use LTOT, suggesting that the potential physical constraints of being connected to oxygen tubing for much of the day do not cause patients to be more sedentary.

Measuring levels of physical activity in COPD patients with accelerometers offers additional information about patients that may help to determine prognosis and appropriate management. However, further work is needed to determine clinically relevant measures and clinically significant changes.

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GLOSSARY OF ABBREVIATIONS

6MWT: 6 minute walk test

ACTRITE: Acute Chest Triage Rapid Intervention Team

ADL: activities of daily living

AW: Actiwatch

BMI: body mass index

BODE Index: Prognostic grading system comprising the body-mass index (B), degree of airflow obstruction (O), functional dyspnoea (D) and exercise capacity (E)

BTS: British Thoracic Society

COPD: Chronic Obstructive Pulmonary Disease

CRQ-SR: self reported chronic respiratory questionnaire

DP: DynaPort

ESWT: endurance shuttle walk test

FEV_1: forced expiratory volume in 1 second

FFM: fat free mass

FVC: forced vital capacity

GOLD: Global Initiative for Obstructive Lung Disease

HAD: hospital anxiety and depression scale
HADa: anxiety score
HADd: depression score

IC: inspiratory capacity

ICS: inhaled corticosteroid

ISWT: incremental shuttle walk test

KCO: carbon monoxide transfer coefficient

LABA: long acting beta agonist

LAMA: long acting antimuscarinic

LCADL: London chest activities of daily living questionnaire

LLN: lower limit of normal

LTOT: long term oxygen therapy

MET: measure of energy expenditure. 1 MET is defined as the energy expenditure for sitting quietly

mMRC: modified Medical Research Council dyspnoea scale (scale 0-4)

MRC: Medical Research Council dyspnoea scale (scale 0-4)

MVC: maximum voluntary contraction

NEADL: Nottingham extended activities of daily living questionnaire

NHANES I Study: National Health and Nutrition Examination Survey Part I

$PaCO_2$: partial pressure of carbon dioxide in arterial blood

PaO_2: partial pressure of oxygen in arterial blood

PR: pulmonary rehabilitation

QF: quadriceps force

RV: residual volume

SGRQ: St George's respiratory questionnaire

TLC: total lung capacity

TLCO: transfer factor of the lung for carbon monoxide

WHO: World Health Organisation

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Chapter 1: Introduction

1.1 Physical activity and health

Physical activity is, and always has been, a part of daily life. Although humans are regarded as cerebral beings, the human body is constructed in such a way as to carry out physical activity in an efficient manner. In the past, physical activity was a necessity for survival; in the more recent past, people have been required to work to earn a living, and this in itself has often involved strenuous labour. More recently, machinery (at home and in the workplace) and motorised vehicles have alleviated many demands on us for physical activity. Moreover, the ever increasing use of technology, particularly in the form of televisions and computers, has lead to us becoming more sedentary than we used to be. In view of this, and the obesity epidemic that the developed world is facing, governmental and non governmental agencies are investing large resources in trying to encourage us to be more physically active(1, 2).

Physical activity is defined as any movement of the body produced by skeletal muscles that consumes oxygen(3). Daily physical activity is the totality of this movement during everyday functioning. Regular physical activity reduces the risk of heart disease, stroke, hypertension, bowel cancer, type 2 diabetes, breast cancer and obesity(4-6). Regular physical activity also alleviates established chronic diseases and reduces the risk of developing functional impairment (7-9). Additionally, physical activity reduces stress and anxiety and improves psychological well-being(10) and appears to reduce the rate of cognitive decline in older adults (11). It is recommended that people undertake at least 30 minutes of moderate physical aerobic activity at least 5 days per week to maintain fitness(4, 12). Table 1.1 outlines some common physical activities and the associated energy expenditure.

Table 1.1: Average energy expenditure for common daily activities for a 70kg adult age 30-50 years (men) and 20-40 years (women). Moderate activity is classed where energy expenditure is between 3.0-6.0 METs. Adapted from Ainsworth et al Compendium of Physical Activities(13)

ACTIVITY	Energy cost (METs)*
Sleeping, lying	0.9
Sitting quietly	1.0
Standing quietly	1.2
Walking at a brisk pace (3-4.5 mph on the level)	4.0
Cycling on the level at 5-9mph	4.0
Fast ballroom dancing, modern dancing	5.5
Playing golf	4.5
Fishing from river bank, standing	3.5
Swimming at recreational pace	6.0
Bowling	3.0
Gardening: raking, shoveling, weeding, planting, pushing lawn mower	4.0-5.0
Housework: mopping, washing windows, cleaning gutters	4.5-5.0
Housework: sweeping indoor floors, dusting, washing dishes, cooking, ironing, making the bed	2.0-2.5
Washing the car	4.5
Sitting, reading a book or newspaper	1.3
Getting dressed and undressed	2.5
Showering, toweling off	4.0
Food shopping with grocery cart	3.5
Carrying groceries upstairs	8.0
Sexual activity	1.0-1.5

*Activities are classified as multiples of 1 MET. 1 MET is defined as the energy expenditure for sitting quietly

Although many people reach the recommended target of physical activity through performing usual daily and occupational activities, more than 50% of American adults do not achieve this(14). Moreover, physical activity tends to decrease with age and in patients with chronic illness- the very people who probably stand to gain the most from regular physical activity(15). This is particularly important in chronic diseases that tend to affect the elderly, such as COPD.

1.2 Chronic Obstructive Pulmonary Disease (COPD)

COPD is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases(16). It is predominantly caused by smoking(17) although occupational dusts, vapours, gases and fumes(18) and atmospheric air pollution(19) can contribute to its development. Although COPD is seen as a disease of late adulthood, there is evidence that lower birth weight and respiratory infection as an infant impact adversely on lung function as an adult(20). It is thought that 15-20% of COPD cases are attributable to occupational exposures(21). In the developing world, there is a high prevalence of COPD among non smokers, and this is largely attributed to the burning of biomass fuels in poorly ventilated homes(22). Although smoking is the main risk factor for COPD, it is estimated that the contribution of the various smoking habits accounts for only 15% of the variance in lung function(23); genetic variation probably plays a major role in offering an explanation for why some individuals are more susceptible to cigarette smoke than others. It is thought that genes related to antioxidant activity may be particularly relevant(24). The prevalence of COPD shows wide variation depending on the population studied and the criteria used for defining the disease; in the UK it is estimated that 13.3% of adults over the age of 35 years have lung function tests in keeping with a diagnosis of COPD, the majority of whom have not been previously diagnosed (25). COPD is the fourth most frequent cause of death worldwide and is expected to be the third leading cause of mortality by 2020(26). It is also estimated that, by 2020, COPD will be fifth among the conditions that will be the highest burden to society on a worldwide scale(27).

Common symptoms of COPD are chronic cough with or without sputum, wheeze and chest tightness. The most concerning symptom, and that which limits physical activity and causes functional limitation in most patients, is breathlessness. The breathlessness of COPD is usually exertional, but it tends to progress over time and patients with severe disease may experience breathlessness at rest. Although the degree of breathlessness and functional limitation are most relevant for the patient, the diagnosis of COPD is confirmed and defined by an objective measure in the form of spirometry. The ratio of the forced expiratory volume in 1 second (FEV_1) to the forced vital capacity (FVC) is less than 70%, and the FEV_1 is reduced. The disease is staged by the FEV_1 expressed as a percentage of predicted for age, sex and race. There are different staging criteria, but the most widely adopted is the GOLD (Global Initiative for Obstructive Lung Disease) staging system, outlined in Table 1.2 (28).

Table 1.2: The 4 stages of COPD as defined by GOLD guidelines

STAGE		FEV 1 (% predicted)
I	Mild COPD	$\geq$ 80%
II	Moderate COPD	50% $\leq$ FEV1 < 80%
III	Severe COPD	30% $\leq$ FEV1 < 50%
IV	Very Severe COPD	< 30% or < 50% with respiratory failure

The GOLD criteria have been criticised by some, with concern that they may lead to overdiagnosis in the middle aged and elderly(29); for this reason, some bodies advocate using an age-specific lower limit of normal (LLN) for the FEV_1/FVC ratio rather than a fixed ratio of 70%. However, using GOLD criteria may offer prognostic benefit; subjects with an FEV_1/FVC <

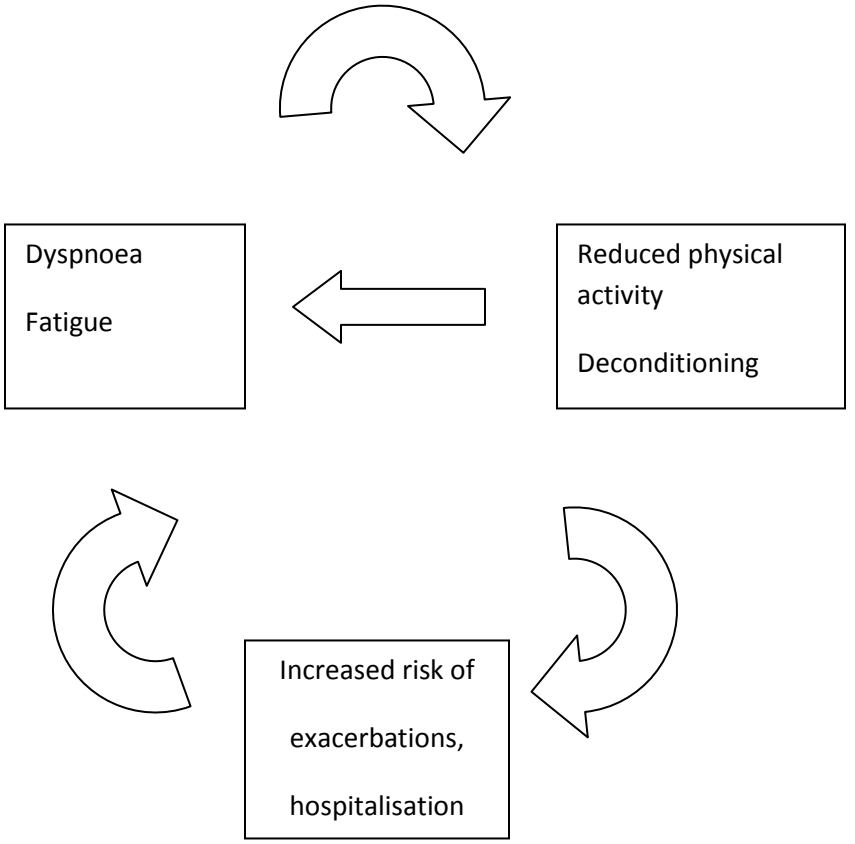
70% but above the LLN appear to have increased risk of death and COPD related hospitalization(30), particularly when accepting an FEV_1 of less than 80% predicted as clinically meaningful(31).

1.3 Physical activity and COPD

COPD is a progressive disease. FEV_1 declines over time as part of the normal ageing process, but this occurs at a faster rate in COPD. Typically, as the disease progresses, patients become progressively more troubled by dyspnoea and fatigue. This will impact on exercise capacity, leading to functional impairment (difficulty in carrying out basic physical or mental actions) and disability (difficulty in performing roles and activities that are normal for that person's age and gender). The disability may relate to difficulty in performing core activities of daily living-ADL's that are necessary for survival, or less essential activities that add quality to life, such as recreational, social or spiritual activities. COPD patients have a ten-fold increased risk of disability compared with healthy adults(32). Initially, COPD patients find it increasingly difficult to perform ADL's that maintain health and wellbeing and fulfill their usual roles. This may mean that the patient needs to modify or give up their job, hobbies or social activities. With disease progression, performing household tasks and leaving the house may become more difficult. Subsequently patients may find it increasingly difficult to mobilise within the house (particularly climbing the stairs) and ability to perform basic self care tasks may also be affected. This worsening functional impairment results in increased periods of inactivity, which leads to adverse structural and biochemical changes in the muscles of ambulation and a decline in physical fitness. This inactivity-induced atrophy is termed deconditioning and makes physical

activity even more difficult to carry out. A vicious cycle of dyspnoea, fatigue, inactivity and deconditioning then develops, accelerated further by exacerbations and hospitalisation (Figure 1.1).

Figure 1.1: COPD- the vicious cycle of dyspnoea, fatigue, inactivity and deconditioning



However, COPD patients are a heterogeneous group and this decline occurs in different patients to different extents, if at all. Some COPD patients have severely impaired lung function, yet have well preserved exercise capacity and maintain their functional status, whereas other patients have

severely impaired exercise and functional capacity, but have only mild or moderate disease based on spirometry. Some of this variation may be attributable to the balance of the underlying aetiology (lung growth impairment in early life, smoking and occupational exposures), the underlying predominant pathophysiology (airway disease versus emphysema) along with the individual's genetic makeup.

1.4 COPD exacerbations and mortality

There are up to 18 definitions of what constitutes a COPD exacerbation, but a widely accepted definition is "an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD(28)." Most COPD exacerbations are triggered by viral or bacterial infections. Exacerbations are associated with increased airway obstruction due to inflammation, bronchospasm and mucus secretion. Exacerbations are a common feature of moderate and severe COPD and impact on the progression of the disease. Not all COPD patients exacerbate, even those with more severe disease, but most do(33). Most exacerbations are managed in the community by general practitioners or self managed by the patient (up to 50% of exacerbations go unreported to health care professionals(34)), but many patients are hospitalized and this is associated with high mortality rates during admission (8%) and at 1 year (23%)(35), higher in more severe disease. Patients who exacerbate frequently have a poorer health-related quality of life(34) and suffer a faster decline in lung function: there is a 25% increase in FEV_1 decline in frequent exacerbators (>2.92 exacerbations per year) compared with infrequent exacerbators

(<2.92 exacerbations per year)(36). A single exacerbation has a large negative effect on health status(37) and recovery of health status and symptoms is prolonged and sometimes incomplete(37, 38). Frequent exacerbations are also associated with increased likelihood of becoming housebound(39) and with increased mortality(40). Frequent exacerbations are associated with more hospital admissions and longer time in hospital(36, 41), which are associated with high social and economic costs. There is considerable interest in which factors predict exacerbation, hospital admission or death in COPD. Poor health related quality of life is associated with exacerbation frequency and readmission(34, 42). Previous hospitalizations, low FEV_1 and underprescription of long term oxygen therapy are associated with increased risk of hospitalization for exacerbation(41), while predictors of readmission for a hospitalization are previous admissions, low FEV_1, hypoxia and lower usual physical activity(43). Impaired health status and exercise capacity are predictive of mortality, independent of FEV_1 and age(44). In more severe disease, decline in exercise capacity is a better predictor of mortality than FEV_1(45). This highlights the relevance of health status, exercise capacity and levels of physical activity in COPD patients.

1.5 Systemic effects of COPD

It is now recognised that COPD is much more than simply a disease of the lungs. The disease is associated with several co-morbidities, independent of smoking status and each other. It is estimated that 50% of COPD patients have 1 to 2 comorbidities, 15.8% have 3 to 4 comorbidities, and 6.8% have 5 or more comorbidities(46). Common comorbities associated with COPD are:

1. Cardiovascular disease: COPD is a powerful risk factor for cardiovascular morbidity and mortality independent of smoking status(47). For every 10% decrease in FEV_1, nonfatal coronary events increase by almost 20%, cardiovascular mortality increases by 28% and all-cause mortality increases by 14%. It is estimated that 20% of patients with stable COPD have concomitant heart failure, probably related to the elevated pulmonary vascular resistance associated with the disease(48).
2. Lung cancer. In a follow up study of 5402 adults over 22 years in the NHANES I Study, there were 113 lung cancers. After adjusting for age, sex, race, education and smoking status (including duration and intensity) the presence of moderate or severe COPD was associated with a hazard ratio of 2.8 for incident lung cancer(49).

FEV_1, independent of smoking habits, predicts death from cardiovascular disease and lung cancer. Cardiovascular disease and lung cancer are important causes of death in COPD. Although most patients with severe disease die from respiratory failure and COPD related causes, cardiovascular disease and lung cancer are the leading causes of death in mild-moderate COPD(50).

3. Osteoporosis. Patients with COPD are at an increased risk of osteoporosis due to their age, limited physical activity, low BMI, smoking, malnutrition and use of oral corticosteroids(51). Even in COPD patients who have never used oral corticosteroids, the prevalence of one or more vertebral fractures is as high as 48.7%(52).
4. Cachexia. Weight loss is a common feature of COPD, and a poor prognostic indicator(53). COPD patients may have a higher basal metabolic rate than individuals without COPD due to the increased work of breathing and underlying systemic

inflammation(54). Moreover, their dietary intake is often poor, particularly when they are breathless at rest. Loss of fat free mass and bone mineral density are linked and greatest with severe lung disease, suggesting common underlying catabolic processes(51).

5. Skeletal muscle wasting. Peripheral muscle wasting is a common feature of COPD, particularly in more severe disease. Chronic inactivity and muscle deconditioning probably contribute to muscle atrophy(55) but the underlying systemic inflammation and oxidative stress of COPD probably also play a role(56), along with frequent oral corticosteroid use and malnutrition associated with the disease.
6. Anxiety and Depression. The prevalence of these conditions is as high as 40% in COPD patients(57) and their presence tends to be associated with increased morbidity and disability and decreased exercise tolerance(58). In more severe COPD, as the patient becomes more restricted in carrying out physical activities and becomes house-bound, the social isolation that results is likely to worsen the situation. Depression in COPD patients is often undetected and untreated(59).

COPD is also associated with type 2 diabetes mellitus, dyslipidaemia and anaemia, and is more frequently associated with pneumonia compared with other chronic diseases(60).

Some of these co-morbidities can be attributed, at least in part, to the low grade pulmonary and systemic inflammation that occurs in COPD(61), markers of which are independent prognostic predictors in COPD(62).

Each of these co-morbidities will have detrimental effects on the patient, contribute to increased mortality(50) and are likely to impact further on reducing exercise capacity and ability to carry out activities of daily living.

The relevance of systemic manifestations in COPD is illustrated in the BODE Index, where a grading system comprising the body-mass index (B), degree of airflow obstruction (O), functional dyspnoea (D) and exercise capacity (E) was more powerful at predicting the risk of death than FEV_1 alone(53). (Table 1.3)

Table 1.3: Variables and point values for calculation of the BODE index (Adapted from Celli et al NEJM 2004(53))

Variable	0	1	2	3
FEV_1 % predicted	≥65	50-64	36-49	≤35
6 min walk distance (m)	≥350	250-349	150-249	≤149
mMRC dyspnoea scale	0-1	2	3	4
Body mass index	≥21	≤21		

A BODE score out of 10 can be calculated for every COPD patient. The hazard ratio for death from any cause is 1.34 and for death from respiratory causes is 1.62 for each one point increase on the scale.

1.6 Limitations to exercise in COPD

As COPD progresses, exercise limitation worsens, leading to reduced physical activity and functional capacity. In health, exercise capacity is limited by a combination of respiratory,

cardiac and peripheral muscle factors, predominantly limited by cardiovascular inability to deliver adequate oxygen to meet demand: the principal symptoms are dyspnoea and leg fatigue. In COPD exercise limitation results from complex interactions between symptoms, impairment of ventilatory and respiratory mechanics, gas exchange abnormalities, peripheral and respiratory muscle fatigue and cardiac dysfunction(63, 64).

1.6.1 Ventilatory limitation

When healthy subjects exercise, expiratory muscles (of which the most important group are the abdominal muscles) are recruited and end-expiratory lung volume is reduced. This results in increased elastic energy in the respiratory system which will aid inspiration and the increased tidal volumes which are required to support increasing exercise. In COPD patients expiratory flow limitation leads to delayed emptying of the lungs during expiration. During exercise, as ventilatory demands increase, the end-expiratory chest wall volume increases progressively and this impinges on inspiratory capacity(65). This is known as dynamic hyperinflation; it increases the ability of the respiratory system to generate expiratory flow but it also results in increased load on the respiratory muscles, increased work of breathing and an increased perception of respiratory discomfort; this may occur in up 80% of patients with moderate-severe COPD(66). Dynamic hyperinflation may occur progressively from the commencement of exercise (early hyperinflators), only in the later stages of exercise (late hyperinflators) or not at all; COPD patients with a greater expiratory flow reserve at rest are able to reduce their end-expiratory chest wall volumes with exercise (euvolaemics). Surprisingly, however, euvolumic patients appear to experience as much exertional breathlessness as hyperinflators, and exercise for less time and

reach lower maximum workloads than hyperinflators(67). It may be that the excessive expiratory pressures generated in euvolaemic patients cause a Valsalva-like effect, reducing venous return and cardiac output; in addition, the high oxygen and energy demands of generating these high pressures would result in a relative reduction in oxygen and energy available for the exercising skeletal muscles. It has been suggested that dynamic hyperinflation develops as the abdominal muscles are de-recruited as an adaptive measure in response to an inadequate supply of energy to meet demands(68). However, as the end-inspiratory lung volume approaches total lung capacity, the inspiratory muscles become functionally weakened and the apparent advantages of dynamic hyperventilation are lost. Rapid shallow breathing is often seen in COPD patients due to increased dead space ventilation and inefficient gas exchange; however, this is an inefficient and wasteful ventilatory method. During exercise, inspiratory effort and central drive increase progressively in the face of increasing difficulty in expanding the tidal volume: this is termed neuromechanical dissociation. These mechanisms result in increased work of breathing and an increased perception of respiratory discomfort in COPD patients. This impacts on their exercise capacity and makes it more difficult to carry out physical activity.

1.6.2 Gas exchange and oxygen delivery limitation

Emphysema is associated with destruction of lung parenchyma. This significantly reduces the alveolar surface area, contributing to ventilation-perfusion mismatching. As a result of the gas exchange limitation hypoxaemia occurs, resulting in reduced oxygen delivery to the exercising muscles. This leads to increased lactic acid secretion (causing skeletal muscle fatigue) and

increased pulmonary ventilation which contributes further to dynamic hyperinflation, further limiting physical activity.

1.6.3 Skeletal muscle dysfunction

Peripheral muscle changes are seen in COPD: muscle atrophy(55), muscle weakness(69) and reduced oxidative capacity(70). The prevalence of lower limb muscle atrophy in COPD is estimated at 21-45%(71). These changes may be mediated via the background low grade inflammation that is associated with COPD(56). Peripheral muscle fatigue occurs and appears to be more marked in the lower limb than upper limb muscles(55, 69). The reduced capacity for aerobic metabolism in the peripheral muscle leads to a switch to anaerobic metabolism, causing increased lactic acidosis for a given rate of exercise(70). Additionally, ventilatory and gas exchange problems, along with reduced cardiac output which is often a feature of COPD, result in decreased oxygen delivery to the exercising muscles, leading to early muscle fatigue and lactic acidosis. The lactic acidosis drives increased ventilatory rates, placing additional burden on the respiratory muscles. COPD patients often state that their exercise capacity is limited by leg discomfort (due to lactic acid accumulation) in addition to breathlessness(72). Additionally, the chronic inactivity that is a recognized feature of severe COPD results in muscle deconditioning, further contributing to the vicious cycle. There is a significant relationship between quadriceps strength and FEV_1 % predicted(55). Exacerbations are associated with a decline in quadriceps strength(73), probably a result of decreased anabolic activity (related to poor nutritional status, reduced levels of physical activity and systemic corticosteroid exposure) and increased catabolic activity (related to increased systemic inflammation, oxidative stress and systemic corticosteroid

exposure)(74). Peripheral muscle strength is a significant determinant of health care utilization in COPD patients(75) and quadriceps strength is a predictor of mortality in moderate to severe COPD(76). There is evidence that physical activity is related to quadriceps strength in exacerbating patients(77), but there does not appear to be a relationship with hand grip strength in stable patients(78).

1.6.4 Respiratory muscle dysfunction

In COPD, the diaphragm adapts to the increased respiratory load and hyperinflation, with a shift from type II to type I fibres (in contrast to skeletal muscle which shows a shift in the other direction(79)) and increased mitochondrial capacity and efficiency (80). However, the hyperinflation that occurs in COPD places the respiratory muscles at a mechanical disadvantage leading to reduced inspiratory muscle strength(81) and reduced ability of the diaphragm to generate transdiaphragmatic and negative intrathoracic pressure(82). This respiratory insufficiency may lead to transient hypercapnia and acidosis during exercise resulting in dyspnoea and increased ventilatory rates, contributing further to reduced exercise capacity. Moreover, these mechanical disadvantages that occur in COPD lead to a high oxygen cost of breathing and competition between the respiratory and locomotor muscles for the available oxygen supply. Any 'steal' of oxygen from the skeletal muscles will further limit exercise capacity.

1.6.5 Cardiac dysfunction

Elevated pulmonary vascular resistance is a recognised feature of COPD. As this progresses, right ventricular overload develops leading to right ventricular failure. Left ventricular dysfunction also occurs due to septal shift. 20% of patients with stable COPD have concomitant heart failure(48). Additionally, air trapping may lead to elevated right atrial pressures and further compromise of cardiac function during exercise(83). There is an association between FEV_1 and cardiovascular mortality, independent of smoking status(84). This may reflect the low-grade systemic inflammation (as suggested by elevated circulating levels of C-reactive protein) which accelerates progression of coronary atherosclerosis, resulting in ischemic cardiomyopathy(85). Impaired cardiovascular function will cause exercise limitation and impact on physical activity.

There is controversy over which of these components is the most important in COPD. Some groups argue that the major limitation to exercise performance is inadequate oxygen and energy supply to the respiratory and locomotor muscles, citing improvement of exercise performance with the administration of oxygen(68). Others attribute the major exercise limitation to lower limb muscle dysfunction based on the structural and energetic changes that occur in the skeletal muscle of COPD patients and the strong correlation of quadriceps strength with exercise capacity, independent of lung function(71, 86). Further weight is given to this argument by the observation that exercise limitation persists for years after lung transplantation(87). Others argue that the main limitation to exercise performance in COPD is dynamic hyperinflation, based on the observation that dyspnoea is usually the symptom which limits exercise in COPD, the correlation of reduced peak oxygen uptake with low resting inspiratory capacity, and the

improved exercise capacity that accompanies the improved inspiratory capacity after the administration of bronchodilators(71, 86, 88, 89). It is likely that activity limitation in COPD is multifactorial and that the components interact with and intensify the adverse effects of each other. For example, a steal phenomenon may occur whereby blood is redirected from the peripheral muscles to the competing respiratory muscles during exercise, leaving both muscle groups with insufficient perfusion and oxygenation(63) and hence exercise capacity is reduced. In addition, each of these mechanisms will feed back centrally leading to increased perception of dyspnoea; the symptom of dyspnoea itself will limit exercise capacity. As discussed earlier, COPD patients may be limited in different ways; for example, they may demonstrate early or late hyperinflation with exercise, or may not hyperinflate at all. Although dynamic hyperinflation is usually seen in moderate-severe COPD, it can also occur in the mild stages of the disease(90), a reflection of the heterogeneity of COPD. All these features are important in COPD since they lead to reduced exercise capacity, which results in reduced daily physical activity.

The importance of the extrathoracic features of COPD is being increasingly recognised. Increased systemic inflammation and left cardiac dysfunction are associated with reduced physical activity in COPD patients, independent of GOLD stage or BODE score(78). Non respiratory functional limitation including body composition and peripheral muscle strength have been shown to be important determinants of disability in COPD patients over and above respiratory impairment(91).

Reduced daily physical activity is related to increased hospitalisation(43) and mortality(92). It therefore follows that management strategies for COPD need to address issues beyond improving lung function. In particular, there is increasing interest in ways of improving exercise capacity and physical activity.

1.7 Management of COPD

The GOLD Guidelines(28) set out the following goals in the management of COPD:

1. Relieve symptoms
2. Prevent disease progression
3. Improve exercise tolerance
4. Improve health status
5. Prevent and treat complications
6. Prevent and treat exacerbations
7. Reduce mortality

1.7.1 Smoking cessation

Smoking cessation in mild disease is associated with improvement in long term mortality(93). Disease progression (FEV_1 decline) is modified by smoking cessation(94), although it is unknown whether this translates to improvement in exercise capacity or performance.

1.7.2 Vaccination

Administration of the influenza vaccine to elderly patients with chronic lung disease is associated with reduced mortality and hospitalisation(95) and reduces exacerbations in COPD

patients(96). Although the pneumococcal vaccine is recommended in guidelines(31), there is a lack of evidence that it reduces mortality or morbidity in COPD patients(97).

1.7.3 Inhaled therapy

Inhaled therapy is the cornerstone of COPD pharmaceutical management. Short acting beta agonists and anticholinergic agents alleviate breathlessness, but there is conflicting evidence as to whether they improve exercise capacity(98). Indeed, some patients (with less hyperinflation) paradoxically reduce their exercise capacity after receiving a short acting beta agonist, seemingly as a result of adopting a physiologically inappropriate breathing strategy(99). Long acting beta agonists and anticholinergics reduce dynamic hyperinflation, increase inspiratory capacity and increase exercise capacity with delay in reaching peak levels of breathlessness(88, 89). Similar improvements in exercise capacity have been seen with the combination of an inhaled corticosteroid and long-acting beta-agonists(100). These combination inhalers have also been shown to reduce exacerbations, slow the decline in FEV_1, improve health-related quality of life and show a trend towards reduced mortality. However, patients receiving these inhalers appear to have an increased risk of clinically diagnosed pneumonia, although this does not translate into an increased mortality, hospitalisation rate or worsening health status(101, 102).

1.7.4 Surgical approaches

Lung volume reduction surgery and bullectomy in carefully selected patients has been shown to improve lung volumes, exertional dyspnoea and exercise performance(103, 104).

Although many of these interventions have been shown to impact on health status and functional capacity, it is less clear whether this translates into improved functional status.

1.7.5 Oxygen

Long term oxygen therapy (LTOT) for hypoxaemic patients has been shown to impact on mortality in COPD(105, 106). In this patient group, supplemental oxygen reduces the risk for sudden deaths, and deaths from arrhythmias and ischaemia. While some groups have reported that LTOT provision is associated with improved health related quality of life(107), others have reported worse quality of life in LTOT patients compared with a similar group of non-hypoxaemic COPD patients(108) and this did not improve once the LTOT was established(109). It is also unclear whether LTOT affects exercise capacity or physical activity: while it is plausible that increased oxygen delivery will enable more physical activity, it is also possible that being attached to the concentrator tubing for the majority of the day will restrict physical activity. Okubadejo reported that LTOT patients were less independent in ADL's than non-LTOT patients, based on self completed questionnaire(110). Sandland reported lower objective physical activity levels in 9 patients receiving LTOT compared with 19 patients who were not receiving LTOT(111). These patients were recruited from the pulmonary rehabilitation (PR)

register. It is not clear which patients had been through PR, and when, which may have introduced bias.

In the UK, ambulatory oxygen is usually available via small oxygen cylinders, although other countries tend to use liquid oxygen, which is more expensive but can support longer durations of use. Administration of oxygen during exercise improves exercise performance and reduces the severity of breathlessness at the end of exercise, even in non-hypoxaemic subjects(112-114). There is also evidence that ambulatory oxygen compared to cylinder air improves health related quality of life in COPD subjects with exertional desaturation, at least in the short term(115). Increasing the inspired oxygen concentration reduces chemoreceptor input, improves operating lung volumes and, by increasing oxygen delivery to the tissues, probably reduces lactic acid secretion in the exercising muscles. In practice, ambulatory oxygen tends to be provided for patients who desaturate on exercise, as recommended by guidelines(31). Although the administration of oxygen has been shown to improve exercise performance in the laboratory, it is not clear whether this translates to improved physical activity at home(116). Moreover, it is not clear how many patients who are provided with ambulatory oxygen actually use it(117).

Although widely used, the benefit of short burst oxygen for symptom relief is not proven and this treatment appears to have a placebo effect rather than a physiological benefit. Giving oxygen before exercise is no better than air in preventing breathlessness occurring(118), and, although oxygen increases inspiratory capacity more rapidly at the end of exercise than does room air breathing, this does not translate into any significant change in the rate of improvement of breathlessness(119).

1.7.6 Pulmonary rehabilitation

Pulmonary rehabilitation (PR) programmes for patients with COPD are well-established as a means of controlling and alleviating symptoms and optimising functional capacity. PR programmes typically include the following components:

a) Patient assessment. This gives the assessor the opportunity to ascertain that the patient is suitable for PR with no contraindications (such as unstable cardiac disease) and is likely to benefit from the programme. It also provides the opportunity to check that the patient understands what is involved and agrees to participate. Patients are also assessed at the end of the programme to judge objective and subjective benefit.

b) Exercise training. This consists of a range of upper and lower limb exercises through which the patient rotates at timed intervals. Plenty of rest periods are incorporated. Training is usually supervised by a physiotherapist and the duration and intensity of the exercises are advanced through the course as tolerated by the patient. Endurance training is an important part of a PR programme; high intensity training has been shown to improve skeletal muscle bioenergetics and exercise capacity(120, 121). A typical exercise session will last for 45-60 minutes and patients will usually attend twice per week. Additionally, patients are encouraged to continue some of the exercises at home (during the programme and after it finishes).

c) Education about the disease. Health professionals and representatives from self help groups talk about COPD, its causes and treatment to enhance understanding of the disease and empower patients to self manage the disease and modify risk factors such as smoking.

d) Nutritional intervention. Dieticians may attend some of the educational sessions. They can offer advice on weight loss to overweight individuals and may provide nutritional advice and supplementation to those with a low BMI (body mass index). Although it is not clear whether nutritional supplementation delivers significant benefits to COPD patients, there is evidence that administration of supplementary polyunsaturated fatty acids in the setting of pulmonary rehabilitation results in additional improvements in exercise tolerance(122).
e) Psychosocial support. This may include breathing exercises to improve respiratory efficiency and cope better with the distressing symptom of breathlessness.

A typical PR programme consists of 2 sessions per week for a total of 6-8 weeks. Most programmes occur in the outpatient setting, although some units provide an inpatient or residential service. Although most PR programmes take place in hospital grounds in the UK, there is an increasing trend for these to take place in the community closer to the patient's home. Most PR programmes are delivered to small groups (8-10 patients) and this allows the patients to support each other. In most units, the PR programme is individualized to the patients' needs.

The main goal of PR is to break the vicious cycle of inactivity, deconditioning and dyspnoea described earlier and restore the patient to the highest possible level of independence. PR is typically offered to patients whose exercise capacity or functional status is significantly impaired by breathlessness, which approximates to an MRC breathlessness score of 3 (dyspnoeic walking at own pace or unable to keep up with contemporaries) although it is likely that all symptomatic COPD patients will gain benefit from a PR programme(123).

Pulmonary rehabilitation improves dyspnoea and fatigue and enhances patients' sense of control over their condition(124). It has also been shown to improve exercise tolerance, functional capacity, quality of life and reduce the number of hospitalizations(64, 125). Although PR has been shown to improve laboratory-based exercise performance (and this parallels improved health status), it is less clear whether PR results in increased physical activity in the home and daily life. Although the benefits of pulmonary rehabilitation compared with control subjects are still seen at 1 year, there appears to be a decline towards baseline in exercise capacity after 6 to 12 months and in health status after 1 to 2 years(126-128). Strategies to maintain the benefits of PR for longer periods include continuing rehabilitation for a prolonged period, maintenance programmes involving continuing home exercises with telephone monitoring, or repeated courses of PR. These strategies may offer modest preservation of the initial benefits of a PR programme, but there is little evidence that they offer significant additional long term benefit(129-132).

1.7.7 Concordance

These management strategies are only effective if the patient takes the medication as directed, uses the LTOT or attends the pulmonary rehabilitation sessions. The WHO (World Health Organisation) estimates that patient adherence to long term therapy in chronic diseases in developed countries is approximately 50%. Concordance rates of this degree are seen in asthma and COPD patients with respect to nebuliser and inhaler therapy(133, 134). There are many reasons for suboptimal adherence, including poor understanding of the disease or treatment by the patient (which may in part reflect poor communication by the healthcare practitioner), difficulty using the provided inhaler device, embarrassment using inhalers or oxygen in public,

and difficulty coping with complex treatment regimens(135). There is some evidence that self-management plans for COPD patients will improve adherence and reduce use of rescue medication, physician visits and healthcare costs(136, 137). However, a Cochrane review of the use of action plans for COPD did not find overall therapeutic benefit in terms of health related quality of life or healthcare utilisation, although patients were better able to recognise and react appropriately to an exacerbation of their symptoms(138).

1.8 Improving physical activity in COPD patients

A relatively high level of usual physical activity is associated with a 46% reduction in the risk of readmission for COPD exacerbation(43), and a level of physical activity equivalent to walking or cycling for at least 2 hours per week is associated with a 30–40% reduction in the risk of COPD related hospital admission and respiratory mortality(139). Possible reasons for this are a better conditioned cardiovascular system being better able to adapt to the increased oxygen uptake in the respiratory muscles that occurs in an exacerbation(140), or an improved oxidative capacity of the muscles leading to better tolerance of an exacerbation(120). In view of these benefits, there is increasing interest in interventions that aim to increase daily physical activity in COPD patients. Indeed the BTS (British Thoracic Society) COPD Guidelines recommend that patients be encouraged to increase their levels of regular physical activity(31). There is also much interest in how daily physical activity can reliably be measured in COPD patients.

1.9 Measuring physical activity in COPD patients

What a subject can do in the laboratory may not be the same as what they actually do at home; this may be different again to what the subject says they can do, and this may be different from what the subject says they actually do. We therefore need to be clear about exactly what we are measuring when assessing physical activity.

1.9.1 Measuring exercise capacity

Objectively measured exercise capacity is often assessed in COPD patients. This may be a cardiorespiratory exercise test on a bicycle or treadmill, or a timed walking test such as the incremental or endurance shuttle walk test, or the 6 minute walk test (6MW). The 6MW is commonly used, since it is cheap and easy to perform; moreover, since a high number of functional activities in daily life involve walking, the 6MW may be a good measure of functional exercise capacity(141). The 6MW correlates well with the more cumbersome maximal exercise test and shows good reliability and responsiveness to change following an intervention such as PR(142). The 6MW offers prognostic information in addition to that provided by spirometry(53). However, measures of exercise capacity are telling us what a patient is capable of doing at a particular point in time in the laboratory; this is not necessarily the same as what the patient is actually doing in their own environment. An intervention may only break the vicious cycle of COPD if it results in increased physical activity, rather than simply the capacity to do more activity. There is increasing interest in measuring physical activity in daily life in COPD patients and the methods with which this can be done.

1.9.2 Direct observation

The only way of knowing for sure what activities patients are performing is by direct observation and recording by a reliable witness. To have an observer sit in a patient's home would be time consuming, intrusive and may lead to altered activity by the patient. Video recording has been used in the laboratory setting, mainly to validate other means of measuring physical activity(143) but the process of analyzing a few days' worth of footage would be labour intensive. Several cameras would be required in each patient's home and it would be difficult to record activity outside of the home. Moreover, the patient may alter their physical activity in the knowledge that this is being scruitinised.

1.9.3 Objective measures of energy expenditure

Indirect calorimetry(144) and doubly labeled water(145) are methods used to calculate energy expenditure. The energy spent on physical activity depends on gender, body mass and movement efficiency and therefore energy expenditure and physical activity are not synonymous, although the terms are sometimes incorrectly interchanged(145). Reliance upon a calorific value as a marker of physical activity can result in under and overestimates when studying individuals within a population. Moreover, these techniques are expensive and burdensome to carry out.

1.9.4 Self reported measures

1.9.4.1 Questionnaires and patient diaries

There are many physical activity questionnaires. Some are specific for COPD, others are more generic. Some assess patients' recall of physical activity performed, while others analyse a patient's ability to carry out specific tasks. These questionnaires then attempt to quantify daily physical activity, which may not be a reliable translation. There are also a number of questionnaires which, although not directly assessing physical activity, are looking at other features of COPD that are related to physical activity.

1.9.4.2 Questionnaires which reflect the level of disablility

The Medical Research Council (MRC) Dyspnoea Scale is commonly used, fast and easy to complete and is a valid method of categorizing the level of disability in COPD patients(146). Subjects are presented with 5 statements relating to the degree of breathlessness with activities and are asked to tick the statement that applies to them. The questionnaire is scored from 1 to 5, with 5 indicating that they are too breathless to leave the house or breathless when dressing or undressing. Sometimes, the modified MRC (mMRC) is used, which uses the same questions, but the scoring is from 0 to 4.

1.9.4.3 Questionnaires which measure health status

Health status is severely impaired in advanced COPD, in part because of recurrent exacerbations but also due to the limitations in exercise performance and the systemic impact of the disease as

it worsens. St George's Respiratory Questionnaire (SGRQ) is a self-completed questionnaire which measures impaired health and perceived well-being in patients with airways disease. Although used as a health related quality of life questionnaire, it includes questions about ability to carry out activities of daily living and one of the four domains by which it is scored relates to activity(147). Although subjects are supposed to self complete the SGRQ, they sometimes struggle with some of the questions (particularly when a response to a double negative is required) and the UK-English version requires a 1 year recall of symptoms. The SF-36 is a commonly used generic survey; in 36 questions it assesses physical and social functioning as well as physical and mental health. The SF36 is a valid outcome measure for COPD patients(148). The self reported chronic respiratory questionnaire (CRQ-SR) is a reproducible, reliable, and stable measure of health status in COPD patients(149) and is sensitive to change after pulmonary rehabilitation(150). The subject selects activities (from a list of 25) that they have carried out (and have experienced breathlessness) in the last 2 weeks and then picks the 5 most important activities. For each activity they select from a 7 point scale the degree of breathlessness that they experience in performing that activity. The remaining 15 questions relate to fear, panic, fatigue and are graded on a 7 point scale expressing the degree of disability. Scores out of 7 are calculated for each domain (dyspnoea, fatigue, emotional, mastery) with a lower score reflecting worse health status.

As previously discussed, anxiety and depression are common in COPD patients(57) and their presence tends to be associated with increased morbidity and disability and decreased exercise tolerance(58). The hospital anxiety and depression scale (HAD) is a self completed questionnaire containing 7 statements relating to anxiety and a further 7 statements relating to depression; a score is obtained for each domain (range 0-21). A score from 8-10 is suggestive of the presence

of anxiety or depression, a score of 11 or more indicates probable presence of the mood disorder. Although designed for hospital general medical outpatients, it is frequently used in primary care(151) and in COPD patients(152).

1.9.4.4 Questionnaires which measure ADL's

Activities of daily living encompass personal care tasks, ambulation, household tasks, recreation and social activities. The core activities of daily living relate to the ability to feed, dress, toilet, wash and bath. While these activities are frequently affected in frail elderly or stroke patients, they are unlikely to be affected in the early stages of COPD. However, instrumental ADL's (IADL's) such as shopping, cooking, housework and transport are more relevant to the wider COPD population, and more likely to show change with treatment(153). A questionnaire which measures ADL's in COPD patients needs to reflect these different components.

The Nottingham Extended ADL (NEADL) Scale is a 21 item self completed scale which asks about the ease with which patients carry out common ADL's. The NEADL was formulated for stroke patients. Although it has been validated in COPD subjects, it includes questions that may not be so relevant in reflecting ADL limitation in COPD (such as reading newspapers and writing letters).

The London Chest Activities of Daily Living Questionnaire (LCADL) asks patients to rate the degree of breathlessness that they would experience on performing various activities relating to self care, domestic duties, physical exertion and leisure; this has been validated in patients with

severe COPD(154). The LCADL consists of 15 activities and can be scored in 4 domains (personal care, household activities, physical activities and leisure activities) but often only the total score is reported (maximum score is 75, with a higher score indicating worse functional impairment). Although the LCADL is a self completed questionnaire, patients have difficulty filling it in. For each activity, a score (0-5) needs to be allocated: many patients assume that the scoring reflects increasing degrees of breathlessness for that activity and complete the questionnaire accordingly. However, this is not the case, and patients often fill out the LCADL incorrectly unless assistance is given; this assistance could introduce bias. Moreover, the LCADL does not allow for particular activities that the patient would not have undertaken, regardless of the chest condition. This means that a subject who wouldn't usually do any of the 15 activities regardless of the chest condition, would score 0 (excellent functional status), whereas a subject who did all 15 activities without breathlessness would score 15, and a subject who became moderately breathless on carrying out these activities would score 30. In addition, a number of questions in the LCADL could be seen as having a gender bias (eg washing hair, making the bed, changing bed sheets) which is important when the scoring does not take account of activities that the subject would not do regardless of their chest condition.

The Manchester Respiratory Activities of daily living questionnaire (MRADL) was designed specifically for use in COPD patients and has shown good validity, reliability responsiveness to pulmonary rehabilitation and is a predictor of mortality in these patients(92, 155).

There are a range of questionnaires and diary methods which look at different aspects of 'activity'. Donaldson looked at diary recording of time spent outdoors in patients with frequent

exacerbations(39), while Garcia-Aymerich (assessing risk factors for exacerbation readmissions) used the Minnesota Leisure Time Physical Activity (MLTPA) Questionnaire and derived calorific measures of energy expenditure(43). However, the MLTPA has been criticised for incompletely assessing walking and stair-climbing activity, which are important activities in COPD subjects and the fact that it requires recall of activities over the previous 12 months(156, 157). A number of questionnaires fail to capture intermittent low level activity and there may be a floor effect whereby the lowest possible score is too high for some subjects(158).

Although questionnaires are cheap and convenient, they do have disadvantages. It is estimated that up to 15% of the UK population is illiterate and health illiteracy may be more prevalent in low income and elderly populations(159). Some questionnaires are difficult to understand with complex language or use of double negatives. For this reason many patients may have difficulty completing such questionnaires reliably. If a relative, friend or healthcare practitioner provides assistance in completing a questionnaire, then bias can be introduced. Patient diaries and most questionnaires depend on a degree of memory recall, which can lead to inaccuracies particularly in an elderly population; recall of light activities (which are important activities in COPD subjects) can be a particular problem(156) and Pitta observed that COPD patients significantly overestimate time spent walking and underestimate time spent standing(143).

Some questionnaires allow an estimate of energy expenditure to be calculated (recall of the duration, frequency and intensity of the physical activity may be required); however, the energy cost of different activities varies from person to person, depending on factors such as body mass and movement efficiency. This limits such questionnaire application in individual subjects. Indeed it has been suggested that the use of physical activity questionnaires should be confined to epidemiological studies(160).

1.9.5 Heart rate monitoring

Since exercise is accompanied by increased heart rate, cardiac monitors could be used to assess for periods of tachycardia as a surrogate for physical activity(161). However, there are many potential confounders. If the patient has coexisting cardiac disease or is on medication such as beta agonists, theophyllines or beta blockers, then this could result in tachycardia or bradycardia. Other conditions such as stress or illness may precipitate tachycardia. Moreover, a deconditioned individual is likely to mount a greater degree of tachycardia for a given activity than a fitter subject. For these reasons, little work has been done in using heart rate as a surrogate for physical activity in COPD patients.

1.9.6 Motion sensors

These devices allow an objective measure of physical activity without the limitation of recall bias, potentially inaccurate completion of questionnaires and the translation of subjective interpretation into objective data.

1.9.6.1 Pedometers

These are small, light devices, usually worn at waist. A horizontal spring-suspended lever arm deflects with vertical movement and a measurement of steps is calculated. Some devices allow a distance travelled to be calculated. These are cheap (£50-£100) and simple to operate and analyse. However, they tend to underestimate slow walking at speeds less than 2mph(162)

although they are more sensitive than self reported questionnaires(163). Most pedometers cannot provide any information on the intensity of movement or the pattern of physical activity. Many pedometers cannot store information beyond the previous 24 hours, so more prolonged readings will require the patient to record the data obtained at the end of each day. For these reasons the majority of studies of motion sensors on COPD patients have used accelerometers.

1.9.6.2 Accelerometers

These devices contain a piezoelectric crystal which is spring loaded with a test mass in contact with the crystal. With acceleration, the force that is applied to the crystal generates a voltage across the crystal; the greater the acceleration the greater the voltage that is generated. The product of frequency and movement intensity (sampled at set intervals) generates an activity count. Accelerometers can measure movements in one (uniaxial) two (biaxial) or three (triaxial) planes. Depending on the device, these can be worn at the waist, hip, back, upper or lower limbs. In contrast to pedometers, accelerometers allow the quantity and intensity of movements to be measured. Percentage of time active and carrying out specific activities can also be calculated, depending on the device. Some accelerometers provide an estimate of energy expenditure; triaxial devices are more accurate than uniaxial(164), although a number of devices have been shown to over or underestimate energy expenditure, supporting the fact that physical activity and energy expenditure are not the same thing. Accelerometers are more sensitive to light activities than pedometers which is an important feature when assessing a sedentary population such as COPD patients. Like pedometers, they can miss certain activities (such as upper arm exercise and cycling) depending on where they are positioned; however, it is widely accepted that walking is the most important type of physical activity in daily life, particularly in the

elderly(165). These devices can usually store data continuously over a period of several days, which relieves the burden to record data at the end of each day. They are, however, more expensive than pedometers (£880 for the Actiwatch, £2200 for the DynaPort). Although more information can be obtained from the triaxial devices, they tend to require more complex software to set up and read; they can also be bulky and cumbersome for the patient to wear and operate.

Depending on the device and where it is positioned, activity counts may be over estimated (vibration detected while seated in a moving vehicle, wheelchair or rocking chair may be interpreted as activity) or under estimated (a device on the arm may fail to detect slow walking).

Although motion sensors do provide an objective measure of activity, patients are aware that they are wearing them and may alter their activity as a result, although there are small studies to suggest that this is not the case(111). Activity monitors can be used to advantage as a way of reinforcing exercise adherence; some motion sensors allow subjects to self monitor their activity levels, allowing them to monitor their progress on an exercise programme.

1.9.6.2a Uniaxial accelerometer: Actiwatch (Cambridge Neurotechnology Ltd)

This device is the size and weight of a wrist watch. It records all acceleration greater than 0.05 times gravitational acceleration and samples the amplitude 32 times per second; it captures the highest amplitude (ie the peak intensity of movement) in that second; this is the activity count for that second. The software can be adjusted to calculate the total activity count in 15 or 30 second epochs. This allows further information to be obtained such as the percentage of time in the day moving.

The Actiwatch (AW) is cheaper and easier to wear and operate than the DynaPort. It can be worn on the wrist or leg, although the latter would be the preferable site since lower limb activity is the major determinant of whole body activity(166). Walker found that there was good agreement between both Actiwatch mean activity score and movement intensity and DynaPort movement intensity. He also demonstrated that the Actiwatch is responsive to an intervention such as pulmonary rehabilitation(166).

1.9.6.2b Triaxial accelerometer: DynaPort (McRoberts)

This device weighs 375g. The main component contains 2 sensors (which measure horizontal and vertical acceleration) and is worn around the waist in a neoprene belt. This is connected via a lead to a sensor strapped to the left thigh which measures vertical acceleration. This allows the type of activity and body position to be characterised. A measure of percentage time spent walking, standing, sitting and lying can be obtained, in addition to movement intensity.

Pitta has done several studies in COPD subjects with this device. He has shown that the DynaPort (DP) is as accurate as video recordings in assessing time spent walking, cycling, standing, sitting and lying in 10 subjects with COPD stages II-IV (intraclass correlation 0.999 for walking time, 0.998 for standing time, 0.77 for sitting time and 0.75 for lying time). He also found that movement intensity correlated with walking speed during fast walking ($r=0.72$, $p<0.05$), but not slow walking ($r=0.21$), although increase in walking speed correlated with increase in DynaPort movement intensity ($r=0.81$, $p<0.01$)(143). A separate study of 50 stable COPD patients showed less time in weightbearing activities (walking and standing) and lower

movement intensity during walking when compared with 25 healthy elderly controls(167). Pitta's group looked at physical activity measured by the DynaPort in 17 patients hospitalised for a COPD exacerbation. Time spent on weightbearing activities was very low during the hospitalisation and 1 month after discharge; in addition, patients with lower activity levels 1 month after discharge were more likely to be readmitted in the following year(77). These patients were all hospitalised for at least 10 days, in keeping with that hospital's clinical pathway, a very different practice to that experienced in UK hospitals, where most patients are discharged within 5 days (particularly if there is a 'hospital at home' scheme in place(168)). Pitta also assessed physical activity in 29 patients after a 6 month course of pulmonary rehabilitation. At 3 months, movement intensity during walking had increased, but not time spent walking; at 6 months, time spent walking had increased at the expense of decreased lying time, and movement intensity had increased further, although standing and sitting times were largely unchanged(169). Most PR programmes currently in practice are for 6-8 weeks, where evidence of improvement in levels of physical activity using accelerometers is conflicting(170, 171); moreover, it is not clear what happens to levels of physical activity with time after the PR programme has finished.

The DynaPort does have disadvantages. Subjects may find it cumbersome to put on and uncomfortable to wear; they also need to follow several steps in setting the device up. Due to slippage of the device, it can misrepresent lying and sitting time in obese subjects.

1.9.2.6c SenseWear Pro (BodyMedia Inc)

This is a lightweight (82g) biaxial accelerometer which is worn on the upper arm over the right triceps. Multiple physiologic sensors detect galvanic skin resistance, heat flux, skin temperature and near-body ambient temperature. These measures are combined with the accelerometer recordings to generate an estimate of total daily energy expenditure. Energy expenditure estimated by this device correlates well with that measured by exhaled breath metabolic analysis in COPD subjects at walking speeds that would be expected during normal activities of daily living(172). Watz has used this device to demonstrate progressively reduced physical activity through worsening GOLD stages and BODE scores(173), although this was not demonstrated by Pitta with the same device(174). Watz has also used the SenseWear to demonstrate the contribution of extrapulmonary factors (systemic inflammation and left cardiac dysfunction) to reduced physical activity in 170 COPD patients(78).

1.9.2.6d DynaPort Minimod (McRoberts)

This is a new triaxial accelerometer which has the advantage of being smaller and lighter (70g) than the DynaPort. It is as accurate as the DynaPort in detecting time spent walking and in different postures(175).

The Minimod and SenseWear represent a new generation of lightweight activity monitor which provide complementary information on physical activity: The SenseWear was more sensitive at

detecting moderate physical activity than the MiniMod but was less accurate at measuring the step count(175).

1.10 Summary

Physical activity is important in maintaining health and preventing progression of chronic disease. There is increasing interest in the measurement of physical activity in COPD patients, and there are several methods of doing this. Each method has advantages and disadvantages. Accelerometers provide the most accurate measure of objective physical activity. However, accelerometers cannot detect whether an activity is performed with greater ease or less breathlessness in response to an intervention. Therefore subjective questionnaires probably have a complementary role in providing this information. However, accelerometers do have a role in ensuring that we are measuring what the patient actually does rather than what they can do or what they say they can do.

There is increasing interest in the use of physical activity monitors and, as they become smaller and easier to use, their use in research and clinical settings is likely to become more widespread. However, there have been some conflicting studies in relation to the information that actigraphy provides, and there remain a number of unanswered questions.

1.11 Aims of the thesis

In light of the points and uncertainties discussed, this thesis sets out to investigate the following:

1. We aimed to investigate what happens to COPD patients' activity levels when they are hospitalised for an exacerbation in the UK (where a different management protocol is usually followed than for Pitta's Belgian patients).We also wished to compare patients who receive an early discharge with those who remain in hospital. While Pitta reassessed patients 1 month later, we aimed to follow them up over a longer time period. We also aimed to assess whether physical activity levels predict risk of readmission and mortality.
2. In view of some studies showing improvement in physical activity after pulmonary rehabilitation, and some studies showing this not to be the case, we investigated whether COPD patients are more active after a UK 'standard' 8 week course of PR, and whether this is sustained beyond the end of the course or whether this declines, as has been shown for exercise capacity and health status.
3. Since there is a lack of data for benefit from LTOT beyond improved survival, we aimed to investigate whether COPD patients who receive long term oxygen therapy (LTOT) have different levels of physical activity than a group of COPD patients who do not meet criteria for LTOT. We also set out to compare physical activity levels in the group as a whole (as a marker of a more severe but stable COPD group) with a milder set of stable COPD patients.

Chapter 2: Methods

This chapter describes the methods used in the studies carried out in relation to physical activity monitoring. Some but not all of these tests were carried out, depending upon the particular study protocol. Most investigations (except for the home actigraphy readings) were performed in the pulmonary research laboratory at University Hospital Aintree by me. Some tests were carried out by another research doctor or physiotherapist under my supervision. At the initial assessment, a detailed assessment was made of the subject's exacerbation history, co morbidities, medication, smoking status and social history. The subject was also asked about their knowledge of the disease and its causes. A physical examination was carried out at the initial visit. This information was documented on a proforma (appendix). Information relating to exacerbation status and change in medication was recorded on the proforma at subsequent visits (with some additional information, depending on the study protocol).

2.1 Physiological measurements of lung function

Figure 2.1 The Zan body plethysmograph

Readings were taken post bronchodilation: Subjects were given 2.5mg salbutamol via an oxygen driven nebuliser for 5 minutes, with measures of lung function taken 30 minutes later. All measures were taken with the ZAN 530 USB body box (nSpire Health Inc, Colorado, USA) in accordance with international guidelines. The Zan system uses a variable orifice flow sensor and tidal breathing derivation of lung volumes (with temperature compensation) using whole body plethysmography.

a) Measurement of spirometry, slow vital capacity and inspiratory capacity(176)

   Subjects were asked to inhale to total lung capacity and then exhale as quickly and forcibly as possible (forced expiratory volume in 1 second- FEV_1) and continue to complete expiration (forced vital capacity- FVC). At least 3 manoevres were performed until 2 reproducible values (within 10% of each other) were obtained: The highest FEV_1 and corresponding FVC were recorded. Predicted values were based on European Community Coal and Steel scales(177).

a) Measurement of Lung volumes(178)

   To determine slow vital capacity (VC) and inspiratory capacity (IC), subjects were asked to perform tidal breathing into the mouthpiece of the pneumotachograph. They were then instructed to exhale fully (to residual volume) and then to inhale fully to total lung capacity and then to exhale again. The expiratory reserve volume (ERV) was calculated from the first part of the manoeuvre, and the VC was calculated from the second part. The IC was then calculated by subtracting the ERV from the VC. The procedure was repeated until 2 values were obtained from manoeuvres performed with good technique and within 10% of each other; the best reading was used.

In order to measure residual total lung capacity (TLC) and residual volume (RV), subjects performed tidal breathing with the door of the body box sealed closed. A shutter would then momentarily block off the airflow at which point the subject breathed in and then out against the shutter. A measure of functional residual capacity (FRC) was derived, from which TLC and RV were calculated.

b) Measurement of gas transfer(179)

This was derived by fast analysis with a single breath manoeuvre using a gas mixture predominantly of methane and carbon monoxide. Subjects were asked to perform tidal breathing for a few seconds, then they were instructed to rapidly exhale fully and then to inhale fully to total lung capacity and then to hold their breath for 8 seconds, then to exhale fully again, and then inhale. 4 minutes' gap was given between repeat measures to allow carbon monoxide clearance. Where possible, 2 readings within 10% of each other were obtained, the higher reading being used.

Subjects performed all tests at rest, seated and wearing a noseclip. The system was calibrated with a 3l syringe and automatic gas and volume calibration at the start of each day.

2.2 Body mass index (BMI) and Bioimpedance

Subjects were weighed and their height recorded with footwear and heavy clothing removed using calibrated scales and a stadiometer. BMI was calculated as weight (kg) ÷ height $(m)^2$. Although BMI is simple to measure, it can underestimate the nutritional depletion that can occur

in COPD since patients with a relative reduction in muscle mass may still have a normal overall weight. For this reason, measurements of body composition may be more a more meaningful way of assessing patients' nutritional status. A convenient method of determining body composition is with bioimpedance, which works on the principle of different conductance of an electrical current through different body compartments. When an alternating current is passed through biological tissues the resistance consists of two components: the electrical resistance of the material and the capacitive reactance of the cell membrane. At low frequencies (<10 kHz) the cell membrane acts as an insulator and prevents the penetration of electric current into the cell so that current flows predominantly through the extracellular spaces of the tissues. At high frequencies the current penetrates the cell membrane enabling it to pass through both the intracellular and extracellular spaces. In bioimpedance measurements, a small alternating current is applied via two electrodes to the body; the voltage produced is detected by a second pair of electrodes, and the impedance is calculated. A limitation of whole-body biompedance is its inability to accurately assess regional accumulation of fluid, such as when there is significant leg oedema and this may result in inaccurate estimates of fat free mass. Bioimpedance was recorded using the Quadscan 4000 (Bodystat, Isle of Man, UK) with the patient lying in the supine position (having rested for 5 minutes, and fasted for 1.5 hours) with no body parts touching each other and the legs apart. Electrodes were placed just proximal to the metacarpophalangeal joint of the right middle finger, the styloid process of the right ulna, the right middle metatarsophalangeal joint and between the right medial and lateral malleoli. From the impedance, estimates of fat free mass (FFM) were calculated using a disease-specific equation(180). This system automatically performs its own calibration check each time a measurement is taken.

2.3 Questionnaires

Depending on the study, questionnaires administered were the Nottingham Extended Activities of Daily Living (NEADL), MRC dyspnoea scale, Hospital Anxiety and Depression Scale (HAD), St George's Respiratory Questionnaire (SGRQ), Chronic Respiratory Questionnaire -self reported (CRQ-SR), and London Chest Activities of Daily Living Questionnaire (LCADL) in this order. These questionnaires, what they measure and how they are scored have been discussed in Chapter 1. Subjects completed these at rest before carrying out the lung function tests or walking test. They were given as much time as they required and were encouraged to answer the questions independently. However, assistance was provided when required if the subject had difficulty reading or interpreting the questions.

2.4 Assessment of quadriceps strength (Edwards Chair)

Figure 2.2: The Edwards Chair for measuring quadriceps strength

As previously discussed, peripheral muscle weakness is an important feature of COPD. Peripheral muscle weakness is enhanced during an acute COPD exacerbation(73), improves with pulmonary rehabilitation(166) and is a predictor of mortality in moderate to severe COPD(76). Quadriceps force (QF) is a commonly used marker of peripheral muscle strength in COPD since it is a primary locomotor muscle and also because weakness of this muscle is often seen in COPD, in contrast to the skeletal muscles of the upper limbs(181). Quadriceps strength can be measured by assessing non volitional strength using transcutaneous supramaximal magnetic stimulation of the femoral nerve to generate a muscle twitch, the force of which can be measured(181). While this technique allows objective measures independent of the subject's aptitude or motivation, it involves the use of expensive equipment and can cause discomfort to the subject (although the discomfort is less than that experienced with electrical stimulation). An alternative is to measure maximum voluntary contraction (MVC) using the technique described by Edwards(182). We used the original Edwards Chair, which is a rigid chair with upright back support (figure 2.2). Subjects sat in the chair with the pelvis immobilised by a seatbelt secured across the hips. With the hips and knees at 90˚ flexion, a strap was fixed securely above the right ankle with the leg, strap and strain gauge aligned to ensure that the reading was isometric. Subjects were asked to rapidly extend the right knee with as much force as possible and to try to sustain this for 5 seconds. The strap was attached to a strain gauge transducer and the signal was converted via an amplifier (MacLab bridge amplifier, AD Instruments, Sydney, Australia) to generate a measure of force using MacLab Chart and Scope software (Version 3.4). An optimum trace was where there was a rapid near vertical stroke followed by a stable plateau. The trace was visible to the patient and investigator as the manoeuvre was performed, allowing feedback and positive encouragement. The maximum force generated over a 1 second period was recorded in

kg. This was determined by manually selecting 1 second epochs at the peak of each reading; a measure of the mean force over that second was recorded. Subjects performed this manoeuvre at least 3 times (with 1 minutes' rest between attempts) until 2 traces with maximum values within 10% of each other were obtained. The bridge amp was set to zero and the equipment was calibrated with a 20.5kg weight suspended from the gauge beforehand. In subjects where fat free mass was calculated by bioimpedance, a regression equation was used to calculate the predicted MVC value:

56.2 – (0.30xage in years) + (0.68xFFM in kg) – (0.15xheight in cm) – (3.42 if female)(183)

In subjects where fat free mass was not available, MVC was expressed as a function of BMI, where a ratio of <120% is recognised as weak(76).

Figure 2.3: Weak MVC trace for COPD subject with the initial calibration lines visible (set at 0 and 20.5kg)

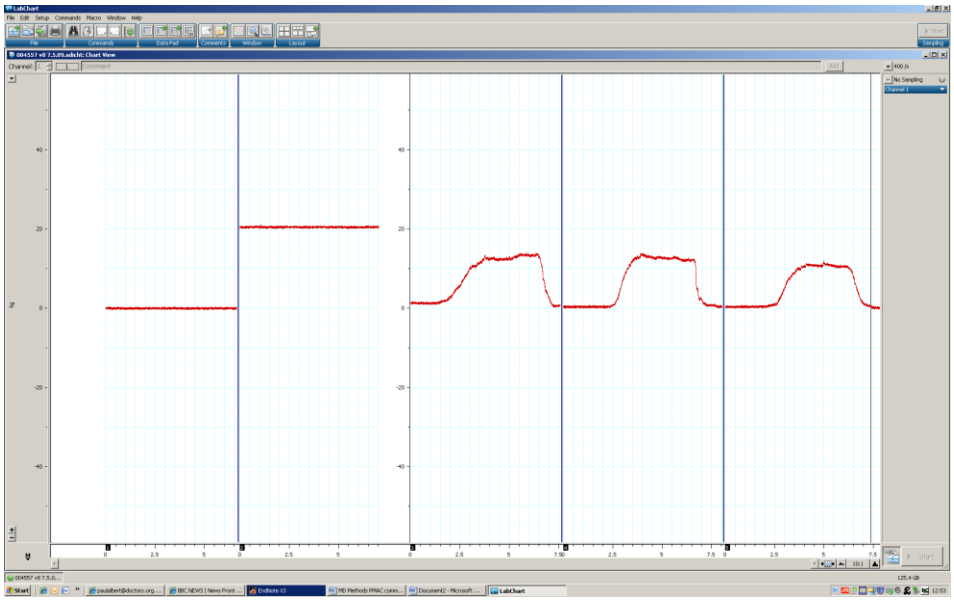
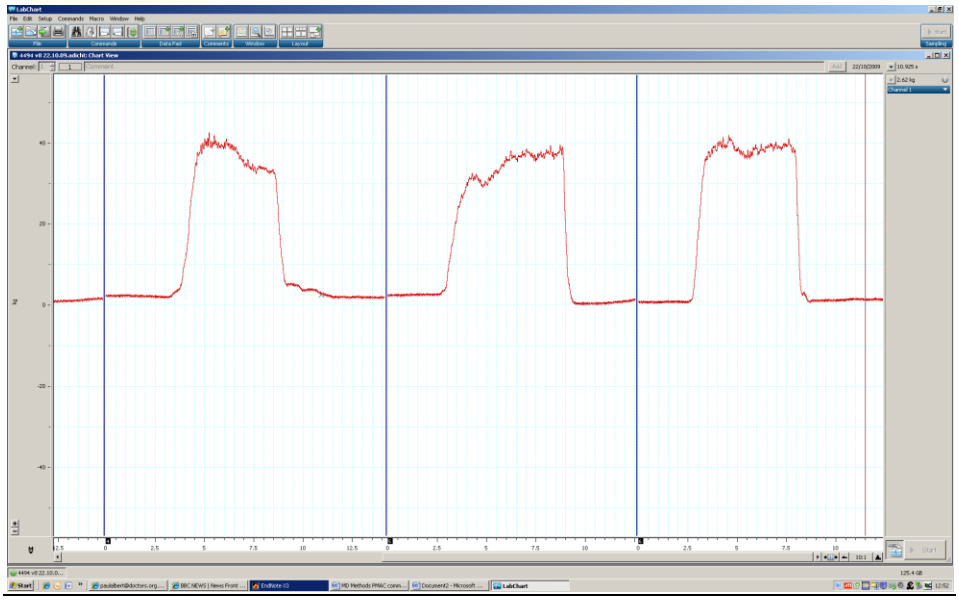


Figure 2.4: Strong MVC trace for COPD subject (baseline at 0kg with peak at approximately 40kg)



2.5 Tests to measure exercise capacity

There are a number of ways of assessing exercise capacity; field walking tests are commonly used. While these do not provide metabolic information that can be obtained from cardiorespiratory exercise testing, walk tests are cheaper and easier to perform and less demanding on the subject, and the information provided has been well evaluated previously.

2.5.1 Six minute walk test (6MW)

In the 1960's a 12 minute walking test was devised to evaluate the physical fitness of healthy individuals(184). Because of the demands of performing a 12 minute test on individuals with disease, the 6 minute walk test (6MW) was developed and was found to perform as well as the 12 minute walk(185). The 6MW is a commonly used test to objectively assess functional exercise capacity; it is easy to administer, well tolerated, is said to be more reflective of activities of daily living than other walk tests(186) and is a prognostic marker in COPD(53). This test was usually carried out after the questionnaires were completed by the patient, ensuring that they were rested before commencing the exercise. Prior to the test, the subject was given verbal instructions to explain what was involved. Subjects were asked to walk up and down a level corridor around two cones placed 19 metres apart (each shuttle walked would be 20 metres). They were instructed to walk as far as possible over a six minute period so as to cover as much ground as possible. They were allowed to pause for rests if required during the 6 minutes, although the clock was not stopped and the subject was asked to restart walking as soon as they were able to. They were accompanied on the walk by the investigator who held a pulse oximeter (BCI International, Wisconsin, USA) with the probe placed on the subjects' finger. Pulse and oxygen saturations were recorded at the start then at 1 minute intervals during the test and 1 minute afterwards for safety purposes: standardised phrases of encouragement were given during the walk. Borg's RPE (rate of perceived exertion) Scale was devised to increase in line with heart rate (ranging from 6-20 to denote heart rates from 60-200 beats per minute.) We recorded The Modified Borg Scale at the start and end of the walk; this is constructed as a category scale with ratio properties(187). Subjects were asked to select their level of breathlessness at the start and end of the walk. A score of 0 would indicate nothing at all; 0.5 would indicate very, very

slight (just noticeable) breathlessness, followed by whole numbers 1 through to 10 (which would reflect very very severe, maximal breathlessness).

The total distance walked in the six minute period was recorded as the sum of the 20 metre shuttles, to give a total distance walked in metres. If the subject completed the test between cones, then the distance walked in that shuttle was calculated to the nearest metre. The 6MW was carried out in accordance with ATS Guidelines(188) with the exception that the subject was also requested to carry out a practice 6 minute walk before the first assessment (due to the learning effect that is seen with repeat tests(189)), with at least 30 minutes' rest before starting the second walk. If the subject was accustomed to using ambulatory oxygen for walking, then this was provided during this test (at the same flow rate that they normally used).

2.5.2 Incremental and endurance shuttle walk

Incremental shuttle walk test (ISWT): This test was developed to simulate a cardiorespiratory exercise test and is a valid field exercise test of functional capacity in COPD patients(190, 191). Subjects were asked to walk up and down a level corridor around two cones placed 9 metres apart (so that the subject walks 10 metres with each shuttle). A Compact Disc was played which sounded an audio cue in the form of a single loud auditory bleep at prespecified intervals and the subject was required to match their walking pace to that of the audio cue. The initial walking speed was very slow (1.80 km/hour) (with the operator walking alongside the subject for the first minute to help establish the starting speed) with progressive increases at 1 minute intervals up to level 12 (8.53 km/hour). The modified Borg dyspnoea scale, pulse rate and oxygen saturations were recorded at the start and end of the test. The subject was requested to walk for as long as

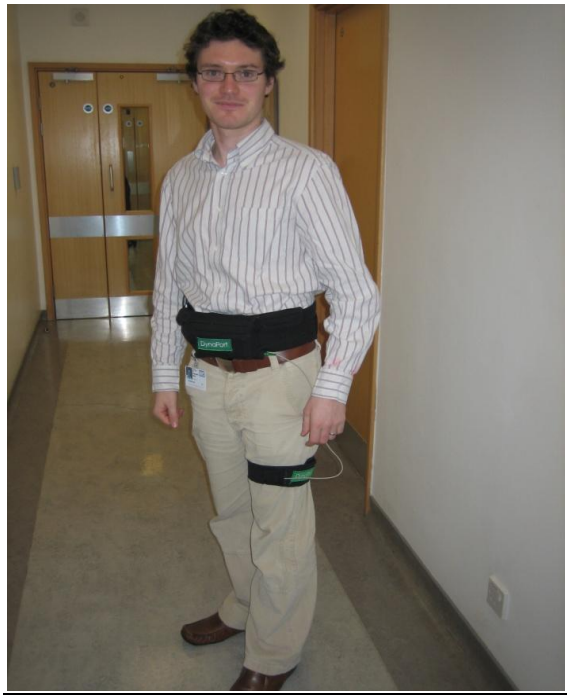
they could until they were too breathless to continue or were more than 0.5m from the cone when the audio cue sounded (having been allowed one lap to catch up). The total distance walked was calculated from the number of completed levels and shuttles and this was used to estimate the subject's peak oxygen consumption (VO_{2peak}) using the following equation:

Predicted VO_{2peak} (ml/min/kg) = 4.19 + (0.025 x ISWT distance)(191)

Endurance shuttle walk (ESWT): This test was developed to complement the ISWT in order to allow endurance capacity at submaximal exertion to be measured in COPD patients. The ESWT is more sensitive to pulmonary rehabilitation than assessments of maximal capacity such as the ISWT(192). There are 16 different levels or walking speeds in this test (from 1.78 km/hour to 6.0 km/hour). The appropriate level was set at a rate that corresponded with 85% value of the indirectly estimated VO_{2peak} calculated from the ISWT(191). After a 90 second warm up (to familiarise the subject with the protocol), audio cues were sounded at a fixed interval (the frequency depending upon the selected level) throughout the test. Subjects were required to complete each 10 metre shuttle before the next bleep was sounded. The test was terminated once the subject was too breathless or unable to keep up with the signals, or if they had successfully managed to sustain their walk for 20 minutes. The total distance walked (excluding the warm up) was recorded. Measures of breathlessness were recorded before and after the test with the Borg Score, and pulse and oxygen saturations were recorded before and after the test using a pulse oximeter. If the subject was accustomed to using ambulatory oxygen for walking, then this was provided during this test (at the same flow rate that they normally used). 30 minutes' rest was allowed between the ISWT and the ESWT. The ISWT and initial ESWT were carried out by a physiotherapist.

2.6 DynaPort activity monitor

Figure 2.5: The DynaPort activity monitor

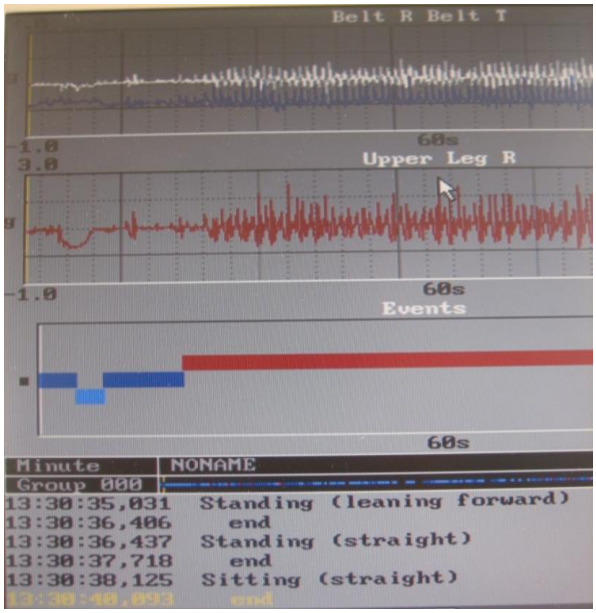


The properties and background behind this triaxial device have been described in the introduction. SD Memory cards were initialised using McRoberts software which operated via Windows DOS. Subjects were provided with full written (instruction leaflet in Appendix) and verbal instructions, with a supervised practice run in the laboratory, for inserting the memory card, putting the device on, fixing the leg sensor on the left upper thigh, powering the device on and starting the reading. Subjects were provided with a 24 hour contact number through which advice and assistance was provided if they had difficulties using the DynaPort at home. They were asked to start using the device first thing in the morning after waking on the day after the laboratory assessment, and to remove it at night before bed. A 24 hour clock was incorporated into the DynaPort so that it was possible to analyse the time periods that the monitor was

measuring over. Depending on the study, subjects were asked to wear this device for 2 or 3 consecutive days. Subjects were asked to wear the DynaPort continuously through the day but to remove it for bathing and visits to the toilet. Although the patient was aware that the monitor was measuring their physical activity, they were asked not to modify their activity because they were wearing the device. Where the device had failed to record for a full day (usually due to battery failure, incorrect device setup or lead disconnection) then the subject was asked to repeat the reading. A set of batteries in the DynaPort would last for up to 2 days: subjects were given a spare set of batteries and shown how to change them. Once the subject had worn the DynaPort for the required number of days a taxi was arranged to collect the monitor from the subject and return it to the laboratory for analysis.

After reading each of the memory cards, the software produced a summary which detailed the total length of reading, the absolute and percentage time spent lying, sitting, standing and walking, along with movement intensity and movement intensity with movement. The full trace could also be interrogated to check that the leads had been correctly placed and to evaluate specific time periods.

Figure 2.6: DynaPort activity trace for COPD subject. The upper bar (white and blue lines) reflects the signal detected by the 2 waist sensors and the middle bar (red line) reflects the leg sensor. The lower bar reports the activity: dark blue (standing), light blue (sitting), red (walking)



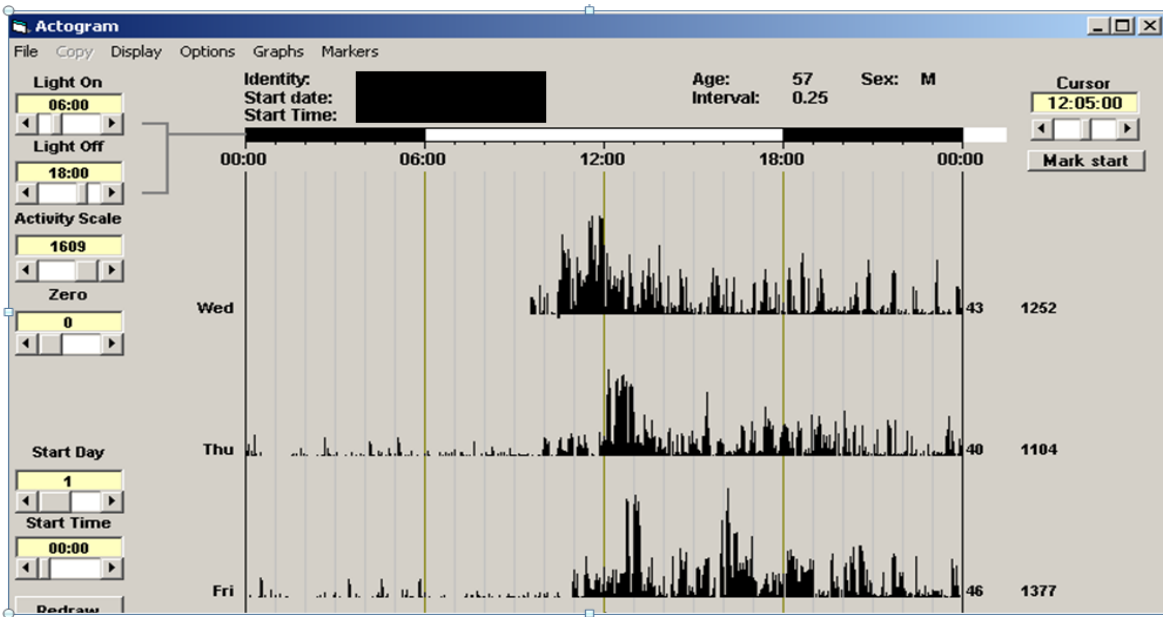
2.7 Actiwatch activity monitor

Figure 2.7: The Actiwatch activity monitor

The properties and background of this uniaxial device have been described in the introduction. The Actiwatch was initialised with a reader/interface device using sleep analysis software (Cambridge Neurotechnology, Cambridge, UK). Subjects were asked to wear the device strapped above their dominant ankle (left ankle if right handed, and vice versa). They were asked to wear the device for 3 consecutive days, commencing the day following the laboratory assessment. Once the subject had worn the Actiwatch for the required number of days, a taxi was arranged to collect the monitor from the subject and return it to the laboratory for analysis. They were asked to put the Actiwatch on first thing in the morning after waking, and to remove it at night before bed. They were given the option to wear the device continuously, in which case they were asked to press the marker button on waking and going to bed each day. They were asked to remove the device for bathing or if they were in significant contact with water. Subjects were asked not to modify their activity because they were wearing the device. The battery life was approximately 3 months, so there was no need to ask the subject to change the batteries.

After reading the Actiwatch, the software produced a histogram illustrating the total level of activity recorded in each 15 second epoch over the period recorded. The histograms were separated into individual days and the data for each day were transferred on to an Excel spreadsheet to allow further interrogation of data. The data were organised to reflect activity through the waking day. Mean activity, percentage time moving and sedentary, mean activity while moving and percentage time performing significant activity were calculated.

Figure 2.8: Actiwatch activity trace for COPD subject. This subject wore the device while in bed on Thursday and Friday, but it is apparent when their waking day started



2.8 Early work with the DynaPort and Actiwatch, and adaptations to study design

Much of the work for this thesis involved the investigation of 3 patient groups using 2 activity monitors, DynaPort and Actiwatch:

A: Stable patients referred for pulmonary rehabilitation
B: Patients recently diagnosed with a COPD exacerbation
C: Patients either on or considered for long term oxygen therapy

We carried out some pilot work in these patient groups in order to evaluate whether patients were able to use the devices, and also to calibrate the Actiwatch against the DynaPort in healthy volunteers and COPD patients in order to obtain additional information on daily physical activity from the Actiwatch.

Our initial work (which will be described in more detail in subsequent chapters) involved actigraphy readings using the DynaPort. We opted for this device due to the additional information that can be obtained over pedometers and uniaxial accelerometers, and its validation in COPD subjects(143).

However, we did encounter some problems with the DynaPort:

A number of subjects reported that they found the device difficult to put on (particularly fastening the waist and leg straps), and found it uncomfortable and cumbersome to wear. Two subjects reported that they were embarrassed to wear the DynaPort outside of the home and that they modified their physical activities accordingly on the days that they were wearing the device (these readings were subsequently excluded from analysis). A number of subjects had difficulty

setting up and switching the device on in the mornings, or placed the leg sensor incorrectly leading to only a partial reading being made (movement intensity and time moving was recorded, but time spent walking, standing, sitting and lying was not). In some cases, the power lead became displaced during the day causing the device to switch off. In 3 obese individuals, the waist belt displaced downwards leading to inaccurate reporting of body position. Incorrect calibration of the monitor (which subjects were required to do when commencing each daily reading) would also result in inaccurate reporting of body position. Additionally, some subjects had difficulty changing the batteries. Some of these problems could be rectified by telephone advice; in some cases it was necessary for the subject to return to the laboratory or a visit to be paid to the subject at home. Incorrect set up, premature device switch off and displacement of a lead or the waist belt were detected when the data were analysed. These data were excluded from analysis and the subject was requested to repeat the readings.

We analysed the number of failed readings and assessed whether COPD severity affected ability to successfully undertake the research protocol.

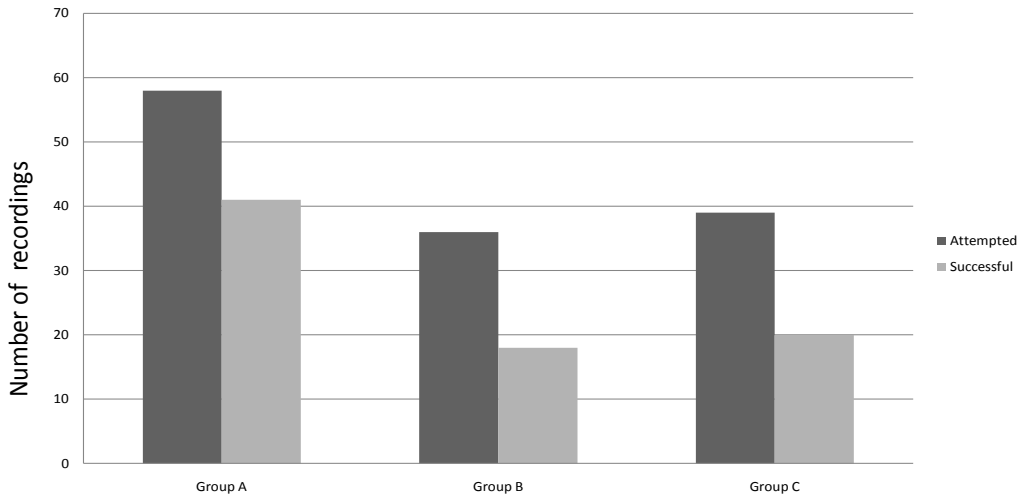
Results

The readings of 29 stable patients referred for pulmonary rehabilitation (group A), 18 patients recently diagnosed with a COPD exacerbation (group B) and 13 patients either on or considered for long term oxygen therapy (group C) were analysed.

Table 2.1: Demographics of the 3 patient groups. A: Stable patients referred for pulmonary rehabilitation, B: Patients recently diagnosed with a COPD exacerbation, C: Patients either on or considered for long term oxygen therapy

	Group A	Group B	Group C
Number	29	18	13
Number Male	12	10	7
Mean Age (yrs)	69.0	67.1	69.8
FEV_1 (l)	1.03	1.08	0.84
FEV_1 % predicted	47.2	45.1	33.5

Figure 2.9: The number of attempted and failed DynaPort recordings by each patient group



In total, there were 133 attempted initial recordings of which 79 were successful and 54 were unsuccessful.

Table 2.2: Reasons for DP reading failure across the 3 patient groups

	Number
Incorrect set up	14
Incorrect placement of leg sensor	21
Inaccurate reporting of body position (slippage of waist belt or incorrect calibration of monitor at set up)	11
Loss of power (battery failure or power lead displacement)	8

29% of initial recordings failed in group A, 50% in group B and 49% in group C. Analysis with one-way ANOVA showed no significant difference between the groups, but there appeared to be a trend towards increased reading failures in sicker and more frail patients (group B and C) than stable patients (group A).

Most patients were willing to wear the monitor again and were able to provide successful subsequent readings. However, the high initial failure rates, along with feedback from subjects about the DynaPort, led us to start using the Actiwatch for the exacerbation and LTOT studies.

2.9 Pilot work and calibration using the Actiwatch

As described previously, the Actiwatch is lighter and easier to wear and set up than the DynaPort. Walker has demonstrated good agreement between Actiwatch (worn on the dominant leg) mean activity score and both % time spent moving and movement intensity measured by the DynaPort(166). However, the data recorded by the Actiwatch are not as comprehensive as the DynaPort; it does not automatically report time sedentary and active, and does not record time spent in different body positions to give a more comprehensive reflection of activities of daily living. However, the raw data provided by the Actiwatch can be interrogated to provide

information beyond the mean activity count. The activity counts provided by the Actiwatch can be analysed in 15 second epochs. For each epoch, if a count of zero is recorded, then no leg movement occurred in that 15 second period, and the subject could be described as inactive in that time period. Thus, by calculating the epochs with no activity and working out the percentage of total time that this represents, then an estimate of percentage time sedentary and active can be calculated. However, minor vibration and minimal leg movement by the subject will generate an activity count, leading to overestimation of meaningful activity by the Actiwatch if we count all readings above zero as 'true activity'(166). We carried out work to calibrate the Actiwatch against the DynaPort in order to determine whether we could establish Actiwatch activity counts that reflected:

1. Low level leg activity. We aimed to determine a threshold that helped distinguish sedentary activity (such as leg movement that may occur while sleeping or sitting or background vibration from a moving vehicle) from low level 'active' activity (which may occur while standing such as waiting in a queue or preparing food in the kitchen).
2. High level leg activity. We aimed to determine a threshold above which high level activities such as walking or running were represented.

This would allow the Actiwatch to provide data that represented time sedentary, time active (low and high level leg activity), time performing intense (high level) leg activity and the mean activity count while active in addition to the mean activity count.

2.9.1 Study 1: Analysis of DynaPort and Actiwatch worn concurrently during a rest/walking exercise using healthy volunteers

9 healthy volunteers (4 male, 5 female: mean age 41 [sd 9.7] years) wore the DynaPort and also the Actiwatch on the dominant leg: the same device was used for each subject. The subjects then followed a timed protocol of rest and incremental walking (stages 2, 8 and 16 of the endurance shuttle walk test with the methods previously described) followed by walking up and down 2 flights of stairs (20 steps). Under supervision, the following protocol was followed:

A: Sitting still [2 minutes]

B: Standing still [2 minutes]

30 second pause

C: Slow walking (endurance level 2) [2 minutes]

60 second pause

D: Normal walking (endurance level 8) [2 minutes]

60 second pause

E: Brisk walking (endurance level 16) [2 minutes]

90 second pause

F: Constant walking up and down 2 flights of stairs (20 steps) [2 minutes]

The data from the DynaPort and Actiwatch for each stage were analysed.

Table 2.3: Range of DynaPort (DP) and Actiwatch (AW) readings for subjects for each stage of activity during a rest/walking exercise using healthy volunteers

Activity	Reading	Range of readings (across all subjects)	Mean reading (all subjects)
A: sitting still	DP % time moving	0.9-6.5	2.5
	DP movement intensity (m/s^2)	0.02-0.13	0.05
	AW activity count*	0-61	2.4
B: standing still	DP % time moving	0.9-4.6	2.2
	DP movement intensity (m/s^2)	0.02-0.05	0.04
	AW activity count*	0-58	4.0
C: slow walking	DP % time moving	86.2-93.7	90.8
	DP movement intensity (m/s^2)	1.34-1.88	1.53
	AW activity count*	282-1280	626
D: normal walking	DP % time moving	93.0-98.6	96.8
	DP movement intensity (m/s^2)	2.67-3.77	3.06
	AW activity count*	617-1924	1376
E: brisk walking	DP % time moving	98.7-99.5	99.0
	DP movement intensity (m/s^2)	3.99-7.03	5.47
	AW activity count*	905-2000	1702
F: stair walking	DP % time moving	97.2-99.1	98.4
	DP movement intensity (m/s^2)	2.87-5.41	4.18
	AW activity count*	679-2000	1513

*The range of readings for the Actiwatch reflects the lowest and highest reading for any 15 second epoch across all subjects during each activity

The broad range of readings at rest (Table 2.3) demonstrates the high sensitivity of the Actiwatch to the most subtle of leg twitches. If we were to use a threshold of zero to differentiate sedentary from active behaviour, then the range for Actiwatch % time active would be 0-42.9 (mean 14.7)% for stage A and 0-63.0 (mean 14.1)% for stage B, depending upon which reading was studied . This demonstrates the need to determine a threshold that reflects meaningful activity. In this group of subjects, it would appear that an Actiwatch count of 61 would be an appropriate threshold to differentiate sedentary from active. However, this study was carried out in the laboratory setting with healthy subjects instructed to sit and stand absolutely still in stage A and

B. Thus, a threshold this low could lead to overestimation of true active behaviour under normal free living conditions. In normal conditions, a subject at rest may fidget or move the legs, generating a transient high activity count while actually being sedentary. On the other hand, a 15 second epoch may include some time of rest and some time of genuine activity: it is important that the period of activity is not overlooked by setting the threshold too high. The range of AW activity counts during slow walking was 282-1280 (mean 626). Since we have categorised any level of walking as high level (intense) activity in our COPD subjects, then we determined that a level of 500 might be an appropriate threshold to differentiate low level from high level activity, although this required confirmation in COPD subjects. As can be seen in Table 3.3 the maximum reading that the Actiwatch can record is 2000; this occurs on some occasions during brisk walking and walking up and down stairs. Whereas this ceiling might be an important factor when assessing intense exercise, it is unlikely to be of importance when measuring routine daily activity in COPD subjects.

2.9.2 Study 2: Detailed analysis of DynaPort and Actiwatch worn concurrently during usual activities of daily living by COPD subjects

5 stable COPD subjects [3 male, mean (sd) age 64 (9) years, FEV_1 1.0 (0.3)l, 41 (22)% predicted] wore the DynaPort and Actiwatch concurrently at home during a normal waking day. Minute by minute analysis of the DynaPort readings was subsequently carried out for each subject. We identified periods of lying, sitting, standing, walking and walking/standing. The periods of walking/standing represented activities such as preparing food in the kitchen, an important aspect of daily life in many COPD subjects that should be captured by accelerometers.

We then analysed the Actiwatch readings and recorded the range of 15 second epoch activity counts reported during each activity. A sample of the ranges is listed in Table 2.4.

In order to reflect intense activity as activity with at least the intensity of walking, we chose 500 as the threshold level for intense activity. Since walking makes up such a small proportion of a COPD patient's day(167) we preferred to set the threshold on the low side so that episodes of low intensity walking are not missed. In order to reflect sitting and lying as sedentary activity, and standing and walking/standing as low level activity, it appeared that a threshold between 0-200 may be appropriate.

Table 2.4: The range of activity count values recorded by the Actiwatch for 5 COPD subjects during various activities (reported by DynaPort)

SUBJECT	lying	sitting	standing	Walking	walking/standing
A	0-119	0-84	0-24	1014-1388	0-866
	2-88	0-280	195-272	972-1141	400-1000
	0-63	0-55	0-201		0-503
		0-168	0-111		0-376
		0-310	0-246		
		0-88	107-299		
		0-68			
		0-195			
B		0-58	0-36	481-948	157-270
		0-25	25-112	622-911	
		0-60			
		0-34			
C	0-55	0-97	71-171	617-906	27-920
	0-71	0-90	8-144	718-996	87-837
	0-32	0-2		315-756	153-629
		0-57			
		0-94			
		0-115			
		0-26			
D	0-52	0-102	188-477	772-1241	0-1241
	0-66	0-115	0-187	934-2000	217-934
				1203-2000	
E	0-15	0-197	0-197	413-811	16-1345
	0-17	0-31	2-178	539-1241	18-613
		0-232			167-983
		0-131			

2.9.3 Study 3: Cross-analysis of DynaPort and Actiwatch worn concurrently during usual activities of daily living by COPD subjects with different thresholds

13 stable COPD subjects [10 male, mean (sd) age 66 (9) years, FEV_1 1.0 (0.4)l, 43 (23)% predicted] wore the DynaPort and Actiwatch concurrently at home during a normal waking day to produce a total of 25 readings. We recorded the % time moving as recorded by the DynaPort. We analysed the Actiwatch readings and, applying different threshold values (0, 50, 100, 150, 200) to differentiate sedentary and active behaviour (expressed as % time active), we assessed which threshold provided the best match for the DynaPort % time moving value. The matrix of data is presented in Table 2.5.

Although 3 readings were closest at a threshold of 50, and 4 were closest at a threshold of 100, the remainder fitted best at 150 or 200. In order not to miss low level activity, we set the threshold at 150.

This work allowed us to obtain additional data from the Actiwatch beyond the activity count. It allowed us to measure surrogates of the same property using either the DynaPort or the Actiwatch. Although the Actiwatch detects leg movement, whereas the DynaPort detects movement of the leg and trunk, this work allows us to estimate % time active and sedentary and also % time carrying out intense activity (as a surrogate for walking) regardless of which monitor was worn by the subject. This allowed us to obtain useful information from the Actiwatch in exacerbating and LTOT assessed patient groups, in which there was a high failure rate when the DynaPort was used.

Table 2.5: Matrix of values for Actiwatch % time active by altering the threshold activity count value

	DynaPort % time moving	Actiwatch % time active				
Actiwatch threshold		0	50	100	150	200
READING						
NO1	1.3	7.8	1.6**	0.7	0.2	0.1
NO2	2.3	11.9	4.6	3.0	2.1**	1.3
EB1	3.4	19.4	11.2	7.5	5.8	4.6**
EB2	3.4	22.3	10.7	7.4	6.1	5.3**
EB3	8.4	31.8	18.7	13.5	10.8	9.6**
EB4	5.5	23.6	14.4	9.5	7.0	6.0**
MF	17.5	51.8	36.4	29.0	22.6	18.3**
BA1	3.4	33.2	8.3	5.0	3.5**	2.0
BA2	4.7	50.8	12.4	7.3	5.2**	3.3
FP1	7.0	56.5	25.0	13.6	9.8	7.5**
FP2	8.1	54.8	22.9	14.1	9.7	7.2**
JR1	10.6	29.6	8.3**	4.7	3.0	1.9
JR2	6.5	21.2	10.2	6.7**	5.1	3.8
JR3	7.8	28.4	12.9	8.5**	5.7	4.2
IC	5.4	38.0	11.2	7.5	5.4**	3.9
DG	20.9	52.1	36.3	29.6	25.2	21.3**
PD1	7.0	38.6	26.3	19.8	15.4	12.6**
PD2	4.2	41.2	26.0	18.4	14.0	11.0**
CM1	14.3	67.0	26.3	17.9	14.4**	12.5
CM2	11.3	55.1	20.9	12.2**	8.3	6.6
PR1	15.6	35.9	16.2**	10.4	8.5	7.7
PR2	14.5	38.8	19.7	14.6**	11.3	9.1
SB	22.8	47.8	33.0	28.0	23.7**	20.8
JM1	7.9	26.6	16.9	12.9	10.5	8.3**
JM2	13.2	37.2	22.7	18.4	16.1	13.9**

**the closest reading to DynaPort % time moving

2.9.4: Sample Size Determination

Since physical activity monitoring is a new research field in recent years, research has tended to be exploratory. Since there are no recognised metrics that reflect clinically significant change of physical activity, it was not possible to calculate required sample sizes for our studies. We tried to recruit as many patients as possible in the timescale allowed, and aimed to recruit numbers that were at least equivalent to those in previous published studies investigating accelerometry in COPD patients.

Chapter 3: Physical activity in patients hospitalised for a COPD exacerbation

3.1 Introduction

COPD exacerbations have been described as respiratory medicine's version of a heart attack. Most COPD patients experience an exacerbation at least once during their lifetime, be it a mild exacerbation (necessitating increased therapy), moderate (when additional medical assistance is sought) or severe (necessitating hospital admission). COPD exacerbations result in worsening health status(34) and accelerated lung function decline(36). Hospitalization for an exacerbation is associated with significant mortality rates, both in the short and long term(35). Following an exacerbation, recovery of health status and symptoms is prolonged and sometimes incomplete(37, 38). Frequent exacerbations are also associated with increased likelihood of becoming housebound(39) and low levels of physical activity are a risk factor for readmission for an exacerbation(43). Frequent exacerbations are associated with more hospital admissions and longer time in hospital(36, 41), which are associated with high social and economic costs. COPD cost the UK economy £492,000,000 in 2003(193), of which 40% was expended on hospital care. COPD exacerbations account for 12% of all acute medical admissions and 15% of all hospital bed days in the UK(194).

In recent years there has been increasing interest in the relationship between exacerbations and physical activity. Garcia-Aymerich et al, looking prospectively at predictors of readmission in 340 patients after hospitalisation for exacerbation identified reduced physical activity based on questionnaire score as a risk factor(43). However, there is uncertainty about the accuracy with which patients might complete a questionnaire and how this reflects actual activity performed in daily life. Pitta used the Dynaport to assess physical activity in 17 patients hospitalised for a

COPD exacerbation(77). Time spent on weightbearing activities was very low during the hospitalisation and one month after discharge; additionally, patients with lower activity levels one month after discharge were more likely to be readmitted in the following 12 months. These patients were all hospitalised for at least 10 days, in keeping with that hospital's clinical pathway, a very different approach to that practised in most UK hospitals. Moreover, the effects of an exacerbation appear to last longer than one month(38), so additional information may be obtained by monitoring physical activity beyond this time. Using the DynaPort and Actiwatch, we aimed to assess physical activity in a group of COPD patients hospitalised with an exacerbation. We aimed to validate the Actiwatch thresholds for % time active and in intense activity in this patient group (previously determined for stable COPD patients in Chapter 2) and then to study individualized and pooled subject data. In a prospective cohort study, the primary aim of this part of the study was to assess levels of physical activity in the early stages of recovery in a group of patients hospitalised for a COPD exacerbation and made comparisons with a similar group of stable COPD subjects.

Some of the exacerbators received early discharge to a 'hospital at home' scheme, known locally as 'ACTRITE' (Acute Chest Triage Rapid Intervention Team). These patients would self administer their current exacerbation treatment (nebulisers, oral corticosteroids and/or antibiotics) at home; they would also be visited by a respiratory nurse on a daily basis, who would assess the patient clinically and check oxygen saturations. Secondary aims of the study were to investigate if there was a difference in physical activity levels between subjects who received early discharge (with or without ACTRITE) compared with those who remained in hospital.

In the next part of the study (Chapter 4), we aimed to track activity levels over the subsequent 4 months of recovery, along with measures of lung function, peripheral muscle strength, exercise capacity and self reported health related quality of life and physical activity based on questionnaires). Finally we assessed whether baseline physical activity or the degree of improvement in physical activity predicted risk of readmission and mortality in the subsequent 12 months (Chapter 5).

3.2 Methods

Patients were recruited from the Medical Admissions Unit and Respiratory Wards of University Hospital Aintree, Liverpool, between October 2007 and October 2008. Patients had been referred to the hospital by the General Practitioner or had self presented at the Accident and Emergency Department. Potential subjects were identified from ward admission lists. Inclusion criteria were a primary diagnosis of a COPD exacerbation by a respiratory physician (based on Anthonisen criteria(195)), and commencement of oral corticosteroids (unless contraindicated) and/or antibiotic therapy. Subjects were approached on day 2-3 of the admission and provided with written information about the study. If they agreed to participate and met inclusion criteria, then the initial assessment was carried out on day 4-6. Exclusions were unstable cardiac or rheumatological disease, significant disease other than COPD, which would significantly affect mobility or daily activity, or significant cognitive impairment. Subjects with acidotic respiratory failure were also excluded. If subjects had suspected COPD without confirmatory spirometry (for example, patients presenting to hospital for the first time), they were enrolled into the study, but were subsequently excluded if post bronchodilator FEV_1 was greater than 80% predicted or if

the FEV_1/FVC ratio was 70% or greater. Participating subjects gave oral and written consent. The study was approved by South Sefton Ethics Committee.

The decision to admit, commence treatment, discharge and initiate ACTRITE discharge was made by the treating medical team without any influence of the patients' participation in the study. If the medical team considered that the patient was suitable for ACTRITE discharge, they were assessed by an ACTRITE nurse who assessed the patient's suitability against a checklist of inclusion and exclusion criteria (Table 3.1) after consideration of the patient's wishes and social circumstances.

Stable COPD patients were recruited from a separate study: these were COPD subjects who had not experienced an exacerbation for at least 4 weeks and who were about to commence a course of Pulmonary Rehabilitation. This subject group will be studied in more detail in Chapter 6.

Table 3.1: Patient eligibility criteria for ACTRITE hospital at home care

Inclusion criteria	Exclusion criteria
COPD confirmed by spirometry	Confusion
pH > 7.35	Suspected underlying malignancy
pO_2 > 6.7KPa (unless oxygen at home)	Pneumothorax
pCO_2 < 8KPa	Uncontrolled left ventricular failure
WCC 4-20 x 10^9	Significant consolidation
Systolic BP > 100mmHg	Asthma
Age > 18	

Visits were carried out in the Respiratory Laboratory at University Hospital Aintree. Transportation to and from the patient's home was provided if they had been discharged from hospital.

Assessment 1 (4-6 days after initial admission date)

A proforma was completed detailing co morbidities, medication, smoking and social history. Measures of height, weight, post bronchodilator spirometry, slow vital capacity and inspiratory capacity were made. Quadriceps force (QF) and 6 minute walk distance (6MW) were assessed. Patients were requested to repeat the 6MW after a rest of 30 minutes (some declined the repeat test due to fatigue). Admission arterial blood gas was recorded. Subjects completed St George's Respiratory Questionnaire (SGRQ), MRC dyspnoea scale, hospital anxiety and depression scale (HAD), London Chest Activities of Daily Living Score (LCADL) and Nottingham Extended Activities of Daily Living Questionnaire (LCADL). Subjects were then asked to wear either the DynaPort (DP) for 2 consecutive days or the Actiwatch (AW) for 3 consecutive days or both monitors. If the patient was discharged to ACTRITE while still wearing the activity monitor, then the recordings were split to reflect the period in hospital and the period at home.

Assessment 2

The aim was for this assessment to be made 1 month after assessment 1. Any exacerbations (requiring oral corticosteroids, antibiotics or both), hospitalisations or changes in treatment (including medication or pulmonary rehabilitation) since the first visit were recorded. Measures of post bronchodilator spirometry, slow vital capacity and inspiratory capacity were made. Quadriceps force (QF) and 6 minute walk distance (6MW) were assessed. Subjects were then asked to wear either DP for 2 consecutive days or AW for 3 consecutive days or both monitors. Due to high exacerbation rates and frailty of many of these patients, a 4 week window was allowed for assessment 2 to be completed.

Assessment 3

The aim was for this assessment to be made 3 months after assessment 1. Any exacerbations (requiring oral corticosteroids or antibiotics or both), hospitalisations or changes in treatment (including medication or pulmonary rehabilitation) since the last visit were recorded. Measures of height, weight, post bronchodilator spirometry, slow vital capacity and inspiratory capacity were made. Quadriceps force (QF) and 6 minute walk distance (6MW) were assessed. Subjects completed St George's Respiratory Questionnaire (SGRQ), MRC dyspnoea scale, hospital anxiety and depression score (HAD), London Chest Activities of Daily Living Score (LCADL) and Nottingham Extended Activities of Daily Living Questionnaire (LCADL). Subjects were then asked to wear either DP for 2 consecutive days or AW for 3 consecutive days or both monitors. Due to high exacerbation rates and frailty of many of these patients, an 8 week window was allowed for assessment 3 to be completed.

Assessments 2 and 3 were carried out when the patient was stable. If the patient had experienced further exacerbations since the previous visit, a window of at least 7 days since completion of the last dose of prednisolone or chest antibiotics was necessary before assessment 2 or 3 could be carried out. Whether the patient wore DP, AW or both monitors was determined by monitor availability and the phase of the study (generally, subjects wore the Actiwatch after the pilot phase was carried out).

Statistical Analysis

Statistical analysis was carried out using SPSS (15.0). Variables were tested for skewdness and Normality using the Shapiro-Wilks test. Mean (sd) values were calculated and non-Normally distributed variables were expressed as median [interquartile range]. Paired data were analysed

by a paired t test or Wilcoxon matched pairs test (non parametric variables). Unrelated data were analysed by an Independent t test or Mann-Whitney test (non parametric variables). Where 3 or more unrelated groups were analysed, comparisons were made using one way analysis of variance (ANOVA) or the Kruskall-Wallis test (non parametric variables). Where 3 or more measures were analysed from the same participants, comparisons were made using one way repeated measures analysis of variance (ANOVA) or Friedman's ANOVA (non parametric variables). When the p value was <0.05 then a post hoc test was performed. A Pearson correlation (Spearman correlation for non parametric variables) test was performed to assess relationships. Survival graphs were demonstrated with Kaplan-Meier plots and factor comparisons were made by long rank analysis pooled over strata. A level of significance was set at 0.05 for all statistical tests, except tests where multiple comparisons were carried out, when the level of significance was set at 0.01. No attempt was made to assume missing data from subjects who were lost to follow up.

3.3 Results

3.3.1 Flow and follow up of subjects

Figure 3.1 shows the progress of subjects through the study. 363 patients were screened, 112 did not meet inclusion criteria and 251 patients were invited to take part. 188 patients declined and 63 patients agreed to take part in the study. 3 patients were excluded on the initial assessment: 2 were excluded due to $FEV_1 \geq 80\%$ predicted and 1 patient was found to have memory problems, leading to difficulties in completing questionnaires and performing spirometry. 28 patients completed assessment 2 (14 patients withdrew after assessment 1 and 18 patients were unable to

complete assessment 2 within an acceptable time frame). 43 patients completed assessment 3: 26 of the 28 patients who completed assessment 2 were able to complete assessment 3 as well as 17 out of the 18 patients who had been unable to complete assessment 2. Sadly, 3 patients died between assessments 2 and 3. As discussed earlier, many of these patients were unable to attend for assessments 2 and 3 at the pre designated follow up times (1 month and 3 months after assessment 1). In order to include as many subjects as possible in the study, the time frames were extended (4 weeks allowed for assessment 2, 8 weeks for assessment 3).

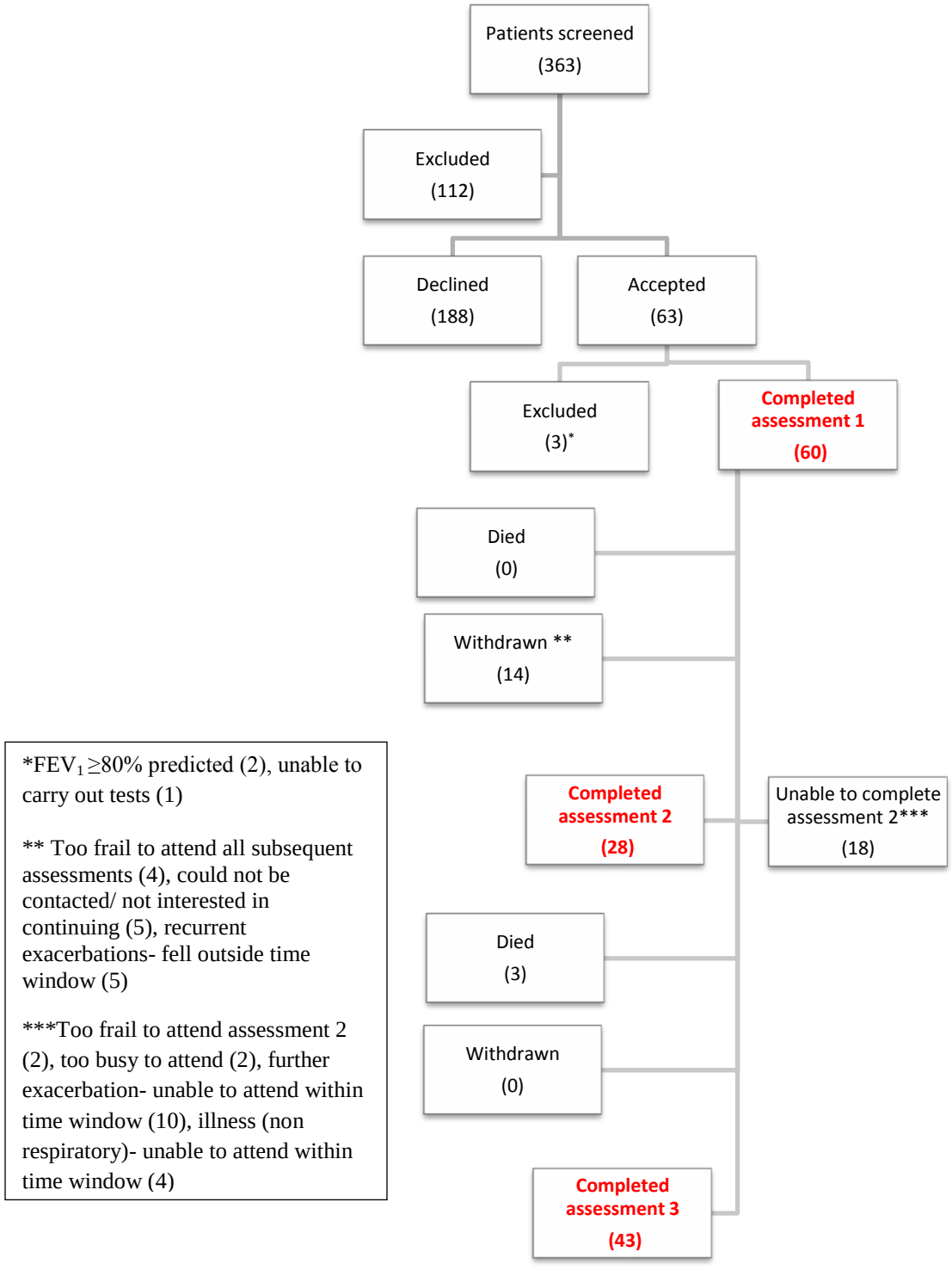
Pharmacotherapy

Of the 60 patients who completed assessment 1, 39 were on triple inhaled therapy (long acting beta agonist [LABA] + corticosteroid [ICS] + long acting antimuscarinic [LAMA]), 15 were receiving only LABA + ICS, 2 were receiving LABA + LAMA, 2 were receiving LAMA only, 1 was on LABA only and 1 subject was receiving no inhaled maintenance therapy. Of the 37 patients in the stable pre-PR group, 29 were on triple therapy, 5 were on LABA + ICS, 1 on LAMA + ICS and 2 patients were receiving ICS only. All subjects also used a prn short acting beta agonist.

Assessment for Normality and Skewdness

Data which were not Normally distributed were QF, MRC, BODE score, DP % time moving, DP % time walking, DP % time lying, AW mean activity score, AW % time active, AW % time sedentary and AW % intense activity. After logarithmic transformation, these variables were Normally distributed with the exception of MRC, BODE score and DP % time lying. All other data were Normally distributed.

Figure 3.1: Flow of participants through the study



3.3.2 Baseline assessment of patients (assessment 1)

The mean (sd) age of the exacerbators was 69.1 (8.9) years. 31 patients were female, 29 male. The mean FEV_1 was 1.0 (0.4) l, 44.7 (17.8) % predicted. Where the arterial blood gas was available, the mean (sd) PaO_2 was 8.1 (1.2) kPa [room air, 23 patients], 10.1 (2.2) kPa [24% O_2, 15 patients], 10.0 (3.2) kPa [28% O_2, 7 patients], 9.4 (2.6) kPa [35% O_2, 4 patients]. 22 subjects were GOLD stage II, 21 were GOLD stage III, and 17 were GOLD stage IV. 59 out of 60 patients who completed visit 1 were receiving oral corticosteroids (30-40mg prednisolone) at the time of the first assessment.

3.3.3 Evaluation of the DynaPort (DP) and Actiwatch (AW) in exacerbators, and validation of Actiwatch measures in this patient group

At assessment 1, 18 patients wore the DynaPort only (the DynaPort failed to record any data for one patient, who was unwilling to repeat the measurement, and only partial readings were made for 6 patients) and 35 patients wore the Actiwatch only. 7 patients wore both monitors simultaneously. Table 4.2 demonstrates the demographics of the subjects who wore DP and AW. There were no significant differences in age, spirometry, quadriceps strength, 6MW or questionnaire scores between the 2 groups.

Table 3.2: Subjects who wore DynaPort (DP) or Actiwatch (AW) at assessment 1

Mean (sd)	DynaPort (n= 24)	Actiwatch (n=42)	p value
Age (yrs)	66.2 (8.7)	70.4 (8.4)	NS
BMI	28.1 (10.3)	28.3 (6.5)	NS
FEV_1 (l)	1.0 (0.4)	1.0 (0.4)	NS
FEV_1 % predicted	43.0 (17.6)	45.4 (19.2)	NS
FVC (l)	2.2 (0.7)	1.9 (0.6)	NS
FVC % predicted	70.5 (18.8)	67.5 (17.9)	NS
QF (kg)*	22.1 [17.3-26.5]	22.3 [17.0-33.1]	NS
QF/BMI % ratio**	95.7 (42.2)	90.5 (39.2)	NS
6MW(m)	192 (106)	153 (93)	NS
BODE	6.4 (2.3)	6.9 (1.8)	NS
$SGRQ_{ACTIVITY}$	82.2 (17.4)	88.4 (9.5)	NS
$SGRQ_{TOTAL}$	69.1 (15.7)	72.9 (13.9)	NS
MRC*	4.5 [4-5]	5 [4-5]	NS
HAD anxiety	9.0 (5.5)	8.6 (4.6)	NS
HAD depression	7.8 (4.8)	8.1 (3.7)	NS
London Chest ADL	39.9 (15.1)	46.6 (14.8)	NS
Nottingham Extended ADL	14.0 (4.5)	11.6 (5.7)	NS
DP % time moving*	7.7 [3.6-12.0]		
DP movement intensity(m/s^2)	0.19 (0.19)		
DP movement intensity during movement	1.87 (0.55)		
DP % time walking*	1.6 [0.4-3.8] [n=18]		
DP % time standing	10.0 (8.3) [n=18]		
DP % time sitting	67.7 (20.7) [n=18]		
DP % time lying*	13.1 [4.0-36.8] [n=18]		
AW mean activity score*		29.6 [14.5-46.1]	
AW mean activity when active		350 (89)	
AW % time active*		5.7 [3.2-9.0]	
AW % time sedentary*		93.6 [91.2-96.9]	
AW % time intense activity*		1.1 [0.2-2.2]	

*Median [interquartile range] (not Normally distributed)
**QF/BMI ratio < 120% is considered weak(76)

Using the methods outlined in Chapter 2, the Actiwatch data was analysed to generate scores for % time active and % time in intense activity. We looked at the data obtained at assessments 1, 2

and 3, where subjects had worn both AW and DP. 7 subjects wore both monitors at assessment 1, 3 subjects at assessment 2 and 10 subjects at assessment 3. Table 3.3 compares the readings for DP % time moving with AW % time active, and DP % time walking with AW % time in intense activity for these subjects.

Table 3.3: Subjects who wore both DynaPort and Actiwatch

Subject	DP % time moving	AW % time active	DP % time walking	AW % time intense movement
20 (Visit 1)	2.0	1.1	0.6	0
22 (Visit 1)	3.4	6.3	1.1	1.3
23 (Visit 1)	2.4	0.6	0	0
30 (Visit 1)	17.5	23.9	7.6	6.3
33 (Visit 1)	4.0	5.0	0.1	0.8
34 (Visit 1)	7.5	11.1	1.6	1.5
35 (Visit 1)	10.6	2.6	1.6	0.1
19 (Visit 2)	23.5	33.0	14.8	10.6
22 (Visit 2)	6.9	9.5	2.1	3.2
35 (Visit 2)	7.8	4.9	2.7	0.7
1 (Visit 3)	17.4	21.4	6.9	7.9
5 (Visit 3)	6.4	6.3	1.9	1.4
10 (Visit 3)	5.4	3.6	1.2	0.7
12 (Visit 3)	13.2	7.0	2.4	2.6
13 (Visit 3)	11.6	15.2	2.9	3.2
16 (Visit 3)	9.8	14.2	2.3	2
18 (Visit 3)	10.7	10.1	5.1	1.3
19 (Visit 3)	13.9	22.1	6.8	4.7
20 (Visit 3)	4.7	6.0	2.1	1.2
22 (Visit 3)	6.3	10.9	3.3	3.3

These readings were plotted against each other and the correlation was calculated. Due to the non parametric distribution of some of these variables, Spearman's correlation coefficient was calculated. AW % time active correlated with DP % time moving ($r = 0.79$, $p < 0.01$) [Figure 3.2]. Bland and Altman plot demonstrated acceptable agreement but increased variability as %

time active increased: this improved when the difference between the 2 readings was expressed as a % of the average [Figure 3.3,3.4]. AW % time in intense activity correlated with DP % time walking ($r = 0.84$, $p < 0.01$) [Figure 3.5] with acceptable agreement on the Bland and Altman plot [Figure 3.6]. Although the correlations were strong, there was some variability in agreement as demonstrated in the Bland and Altman plots. This validation assessment allowed us to use readings from either DP or AW as a measure of % time active or % time in intense activity in these patients (reported as % time active or % time in intense activity), although we acknowledge that they are not measuring exactly the same thing and that the data were distributed non parametrically. We also acknowledge that some of the readings came from the same person at a different timepoint (table 3.3), which means that each measure was not truly independent. However, the aim of this exercise was to analyse one piece of equipment against another and the subject was the vector by which this could be done.

Figure 3.2: Correlation of AW % time active and DP % time moving

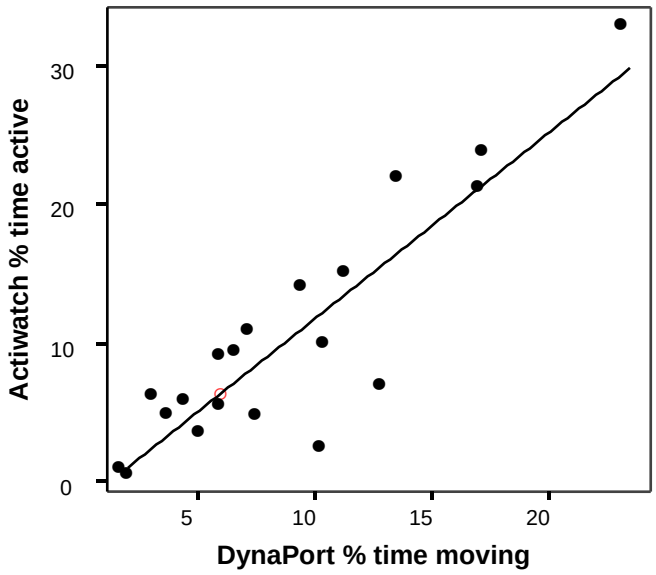


Figure 3.3: Bland & Altman plot of AW % time active and DP % time moving: difference vs average

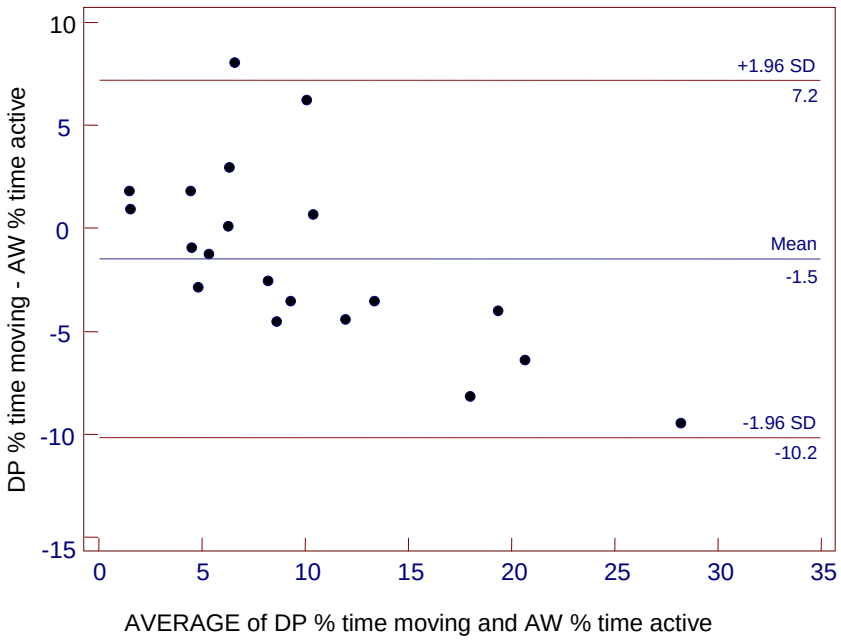


Figure 3.4: Bland & Altman plot of AW % time active and DP % time moving: difference as % of average vs average

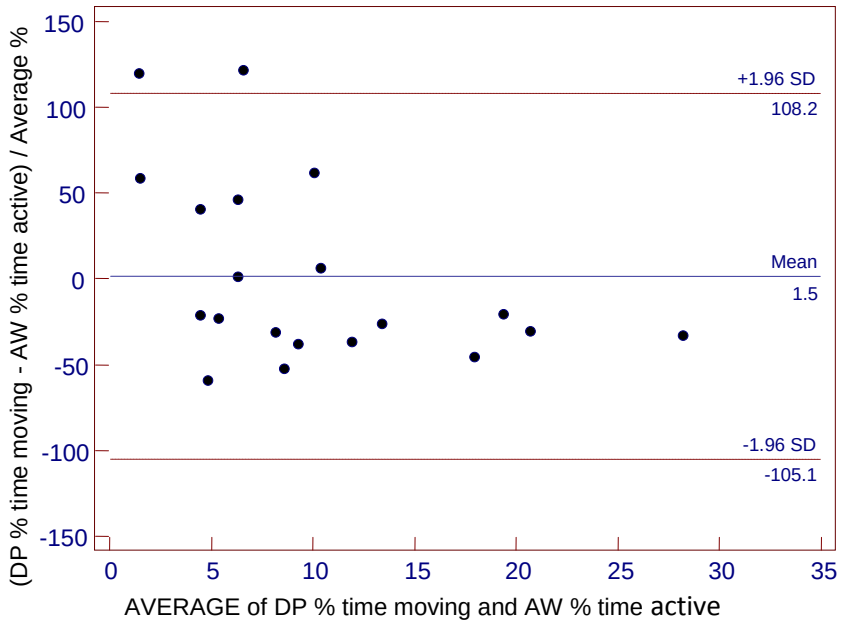


Figure 3.5: Correlation of AW % time in intense activity with DP % time walking

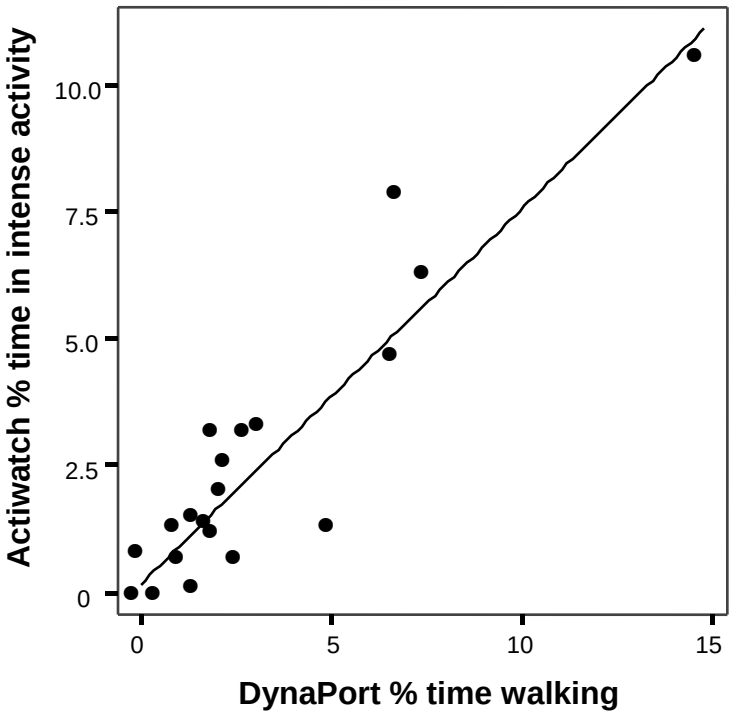
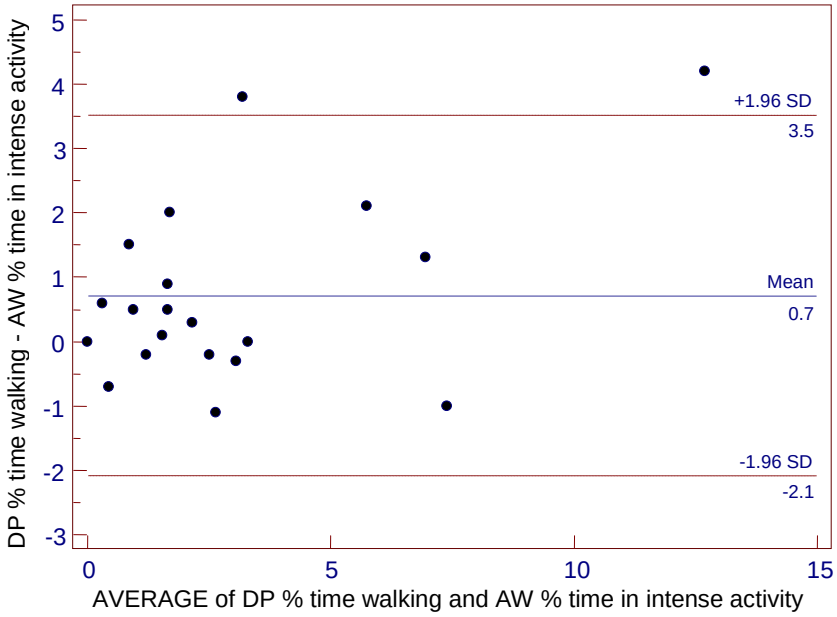
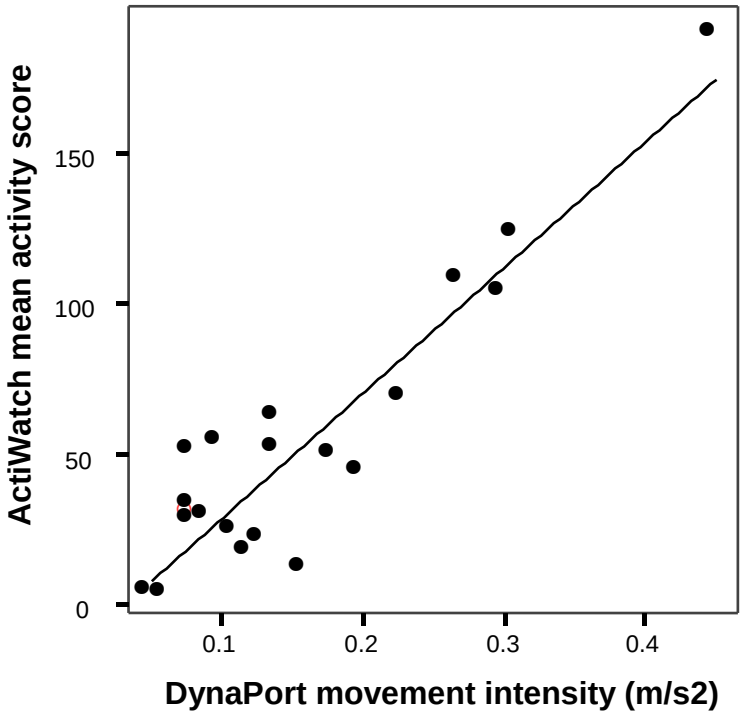


Figure 3.6: Bland & Altman plot of AW % time in intense activity with DP % time walking: difference vs average



The AW mean activity score correlated with DP movement intensity ($r = 0.73$, $p < 0.01$: figure 3.7). The AW calculates the mean activity score as product of frequency and movement intensity, whereas the DP calculates movement intensity (m/s^2). Therefore, the scales are very different and it was not possible to use these data interchangeably.

Figure 3.7: Correlation of AW mean activity score with DP movement intensity



AW mean activity score when active did not correlate with DP movement intensity with movement (figure 3.8). It is not clear from the manufacturer's literature how the DP movement intensity with movement is calculated: there is poor internal correlation with the other DP measurements in contrast to AW mean activity score when active (Table 3.4 and 3.5), which raises uncertainty about the reliability and validity of this particular DynaPort measure. Further analysis using these parameters was not carried out.

Figure 3.8: Correlation of AW mean activity score when active with DP movement intensity

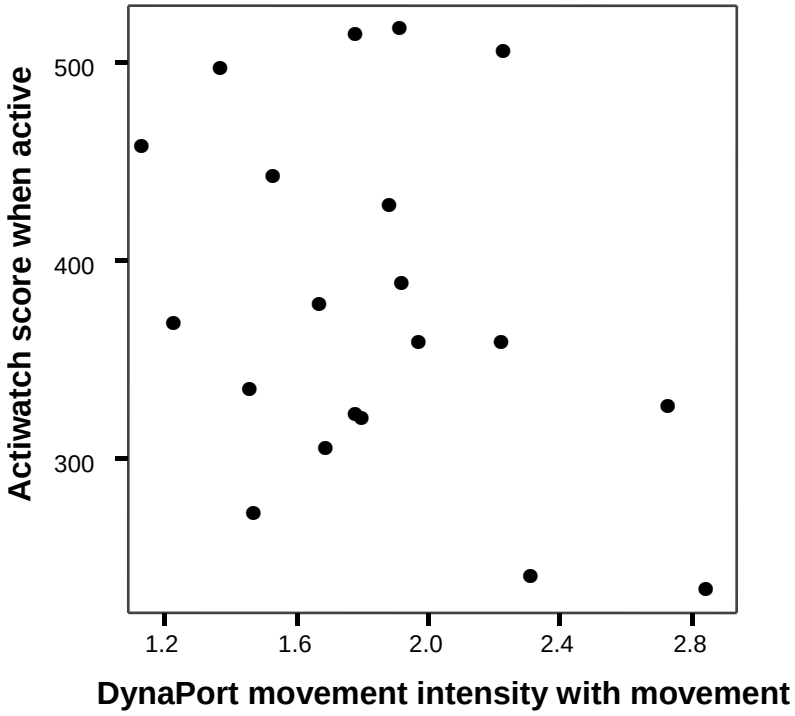


Table 3.4: Internal correlations of measures from AW (20 readings)

	AW mean activity score	AW % time active
AW mean activity score when moving	r = 0.74 (p<0.01)	r = 0.68 (p<0.01)

Table 3.5: Internal correlations of measures from DP (20 readings)

	DP movement intensity (m/s^2)	DP % time moving
DP movement intensity with movement (m/s^2)	r = -0.22 (p>0.05)	r = -0.47 (p=0.04)

3.3.4 Comparison of exacerbators with stable COPD patients and the relationships between FEV_1, reported and actual physical activity, exercise capacity and health status

Table 3.6 compares the exacerbators with stable COPD patients. Age and FEV_1 were similar, although exacerbators had lower FVC (absolute and % predicted). Physical activity (% time active, weight bearing and doing intense activity) was reduced in the exacerbators, although quadriceps force was not statistically different between the 2 groups. Exacerbators also reported significantly worse MRC, SGRQ and LCADL scores. These subjective measures of dyspnoea, health related quality of life and physical activity respectively, did not correlate with actual physical activity in either patient group. This was also the case for all the domains (symptoms, activity, impact and total) of SGRQ. Log quadriceps force correlated with log % time active ($r = 0.38$, $p < 0.01$) and intense activity ($r = 0.43$, $p < 0.01$) in the exacerbators but not the stable patients (figures 3.9-3.12). In the exacerbators, 6 minute walk distance correlated with log quadriceps force ($r = 0.52$, $p < 0.01$, figure 3.13), and there was a weaker but significant correlation of 6MW with log % time active ($r = 0.36$, $p < 0.01$: figure 3.14) but the correlation with intense activity was not statistically significant ($r = 0.35$, $p = 0.02$: figure 3.15). In the exacerbators, log % time active and in intense activity correlated with FEV_1 ($r = 0.43$ and $r = 0.44$ respectively, $p < 0.01$: figures 3.16, 3.17), but the correlation with FEV_1 % predicted was much weaker and not statistically significant ($r = 0.25$ and $r = 0.27$ respectively, $p = 0.06$).

Table 3.6: Exacerbators at baseline in comparison with stable COPD patients

Mean (sd)	Exacerbators (n=60)	Stable (n=37)	p value
Age (yrs)	69.1 (8.9)	67.7 (9.6)	NS
FEV_1 (l)	1.0 (0.4)	1.1 (0.4)	NS
FEV_1 % predicted	44.7 (17.8)	46.9 (16.0)	NS
FVC (l)	2.0 (0.7)	2.4 (0.7)	<0.05
FVC % predicted	69.4 (17.2)	80.1 (16.4)	<0.05
BMI	28.3 (7.7)	26.3 (5.9)	NS
QF (kg)*	21.5 [17.0-31.1]	25.8 [20.1-29.8]	NS
QF/BMI % ratio	90.4 (40.4)	103.8 (31.2)	NS
$SGRQ_{TOTAL}$	71.9 (14.8)	65.6 (14.4)	<0.05
MRC*	5 [4-5]	4 [4-5]	<0.05
London Chest ADL	45.2 (14.8)	34.5 (11.6)	<0.01
Nottingham Extended ADL	12.2 (5.3)	13.4 (4.9)	NS
DP % weight bearing*	9.7 [3.9-18.8] [n=18]	26.3 [17.0-36.2] [n=33]	<0.01
DP movement intensity(m/s^2)	0.19 (0.19) [n=24]	0.20 (0.11) [n=35]	NS
AW mean activity*	27.0 [14.5-49.3] [n=42]	76.5 [42.1-121.2][n=10]	<0.05
% time active*	6.0 [3.4-10.6] [n=59]	9.8 [5.8-14.7] [n=35]	<0.05
% time in intense activity*	1.1 [0.2-2.6] [n=53]	3.7 [2.0-5.7] [n=34]	<0.01

*Median [interquartile range] (not Normally distributed)

Figure 3.9: Relationship between log quadriceps force and log % time active (exacerbators)

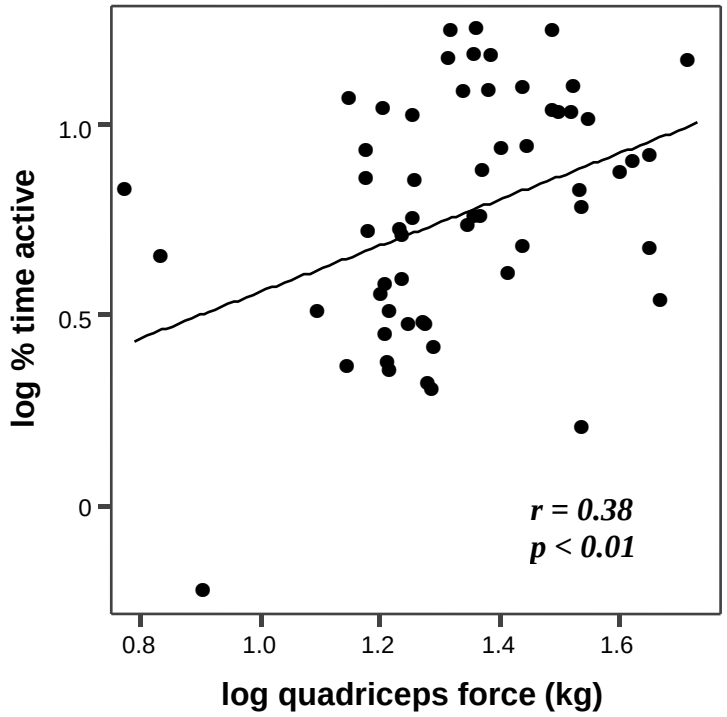


Figure 3.10: Relationship between log quadriceps force and log % time active (stable)

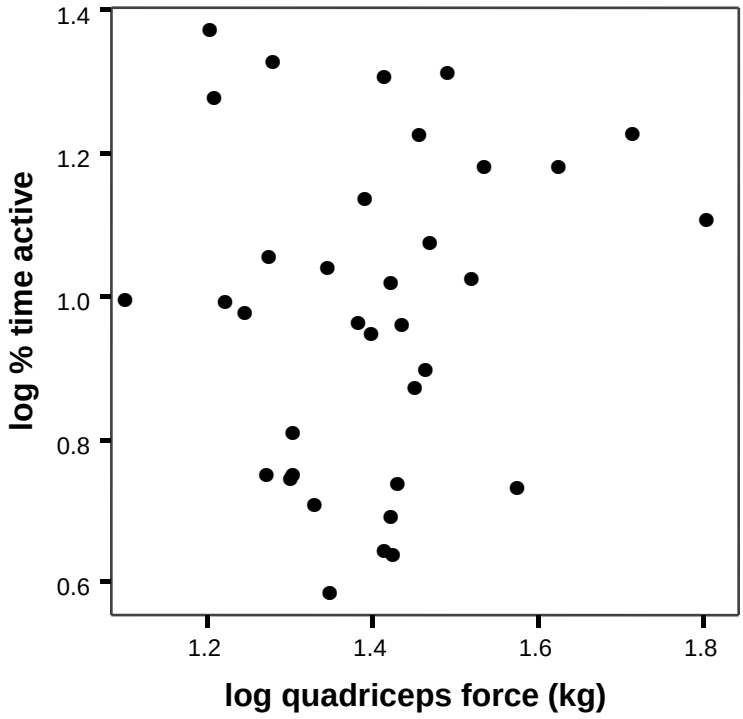


Figure 3.11: Relationship between log quadriceps force and log % time in intense activity (exacerbators)

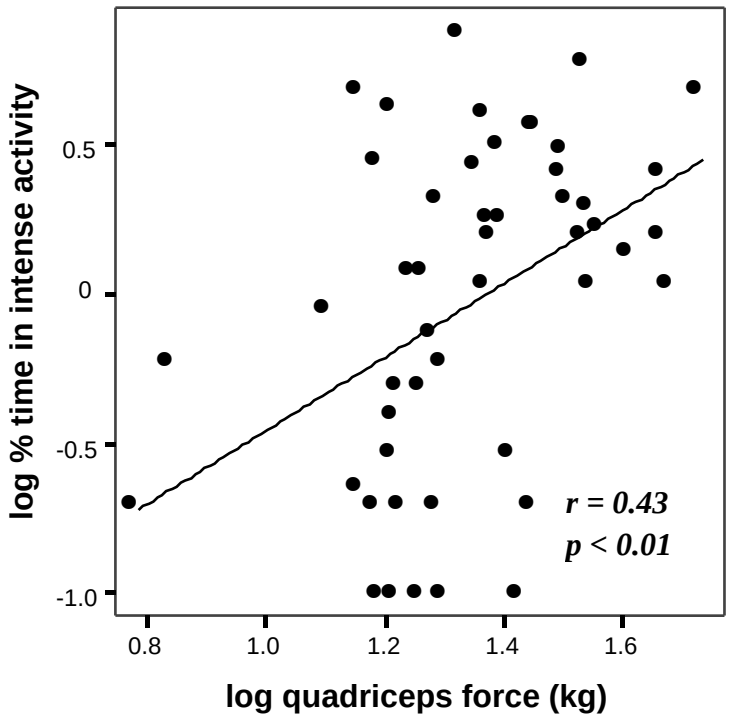


Figure 3.12: Relationship between log quadriceps force and log % time in intense activity (stable)

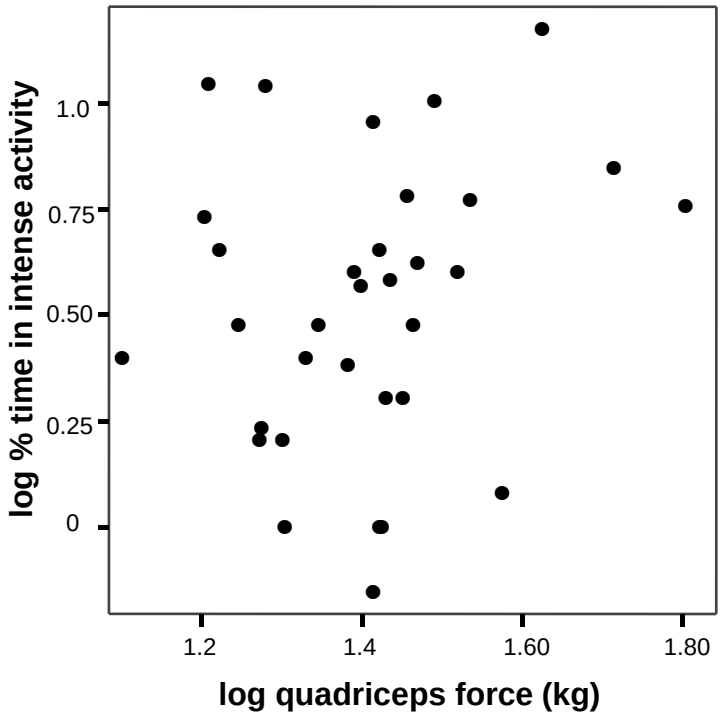


Figure 3.13: Relationship between log quadriceps force and 6 minute walk distance (exacerbators)

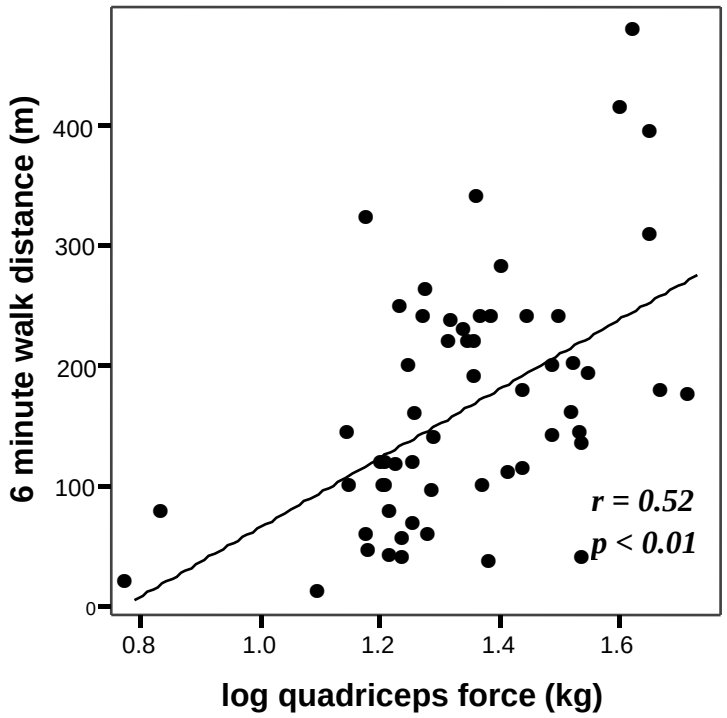


Figure 3.14: Relationship between 6 minute walk distance and log % time active (exacerbators)

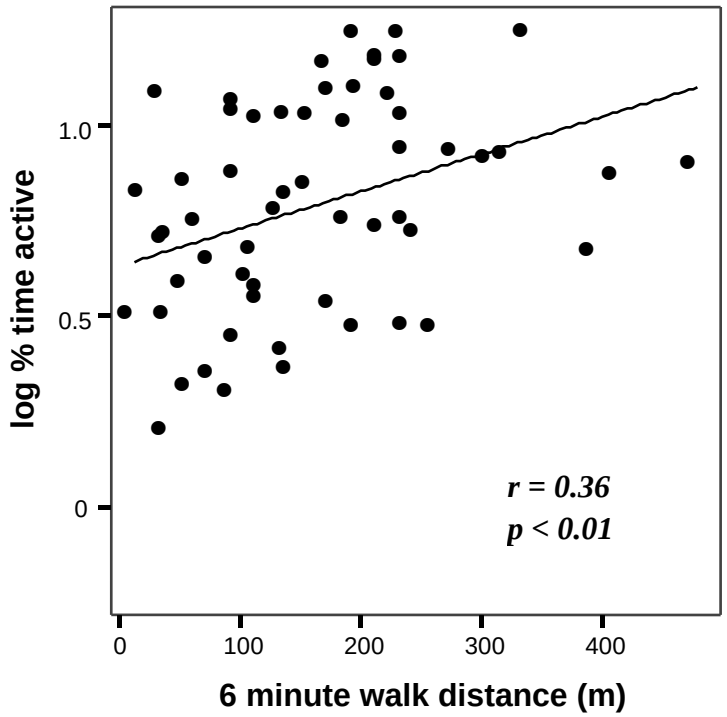


Figure 3.15: Relationship between 6 minute walk distance and log % time in intense activity (exacerbators)

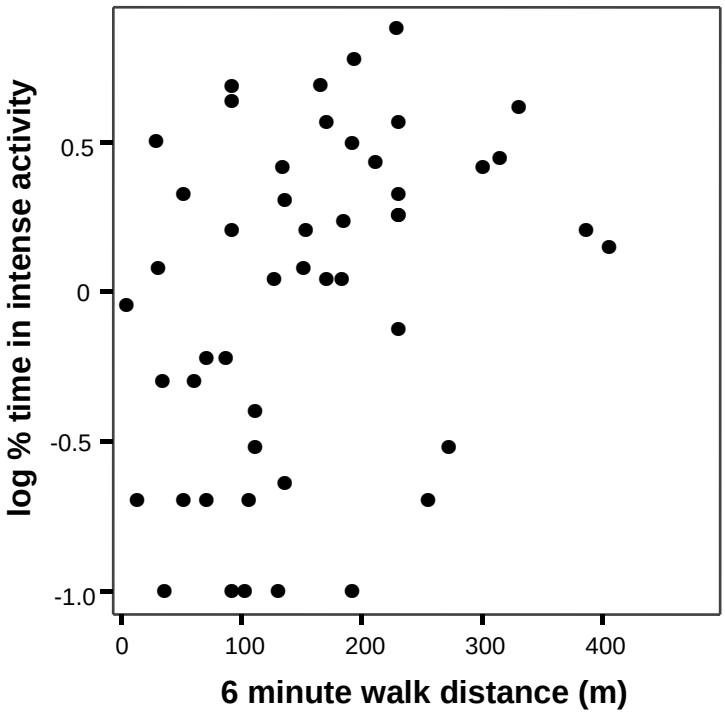


Figure 3.16: Relationship between FEV_1 and log % time active (exacerbators)

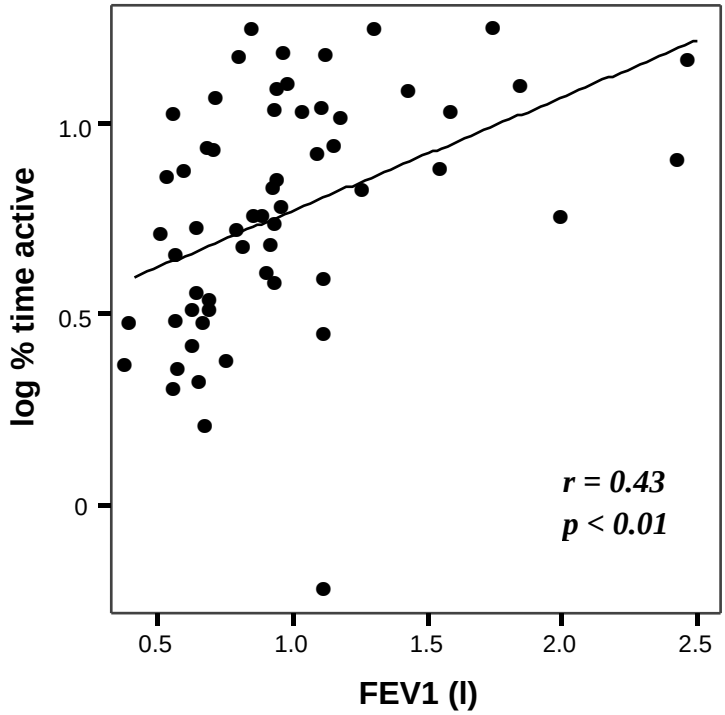
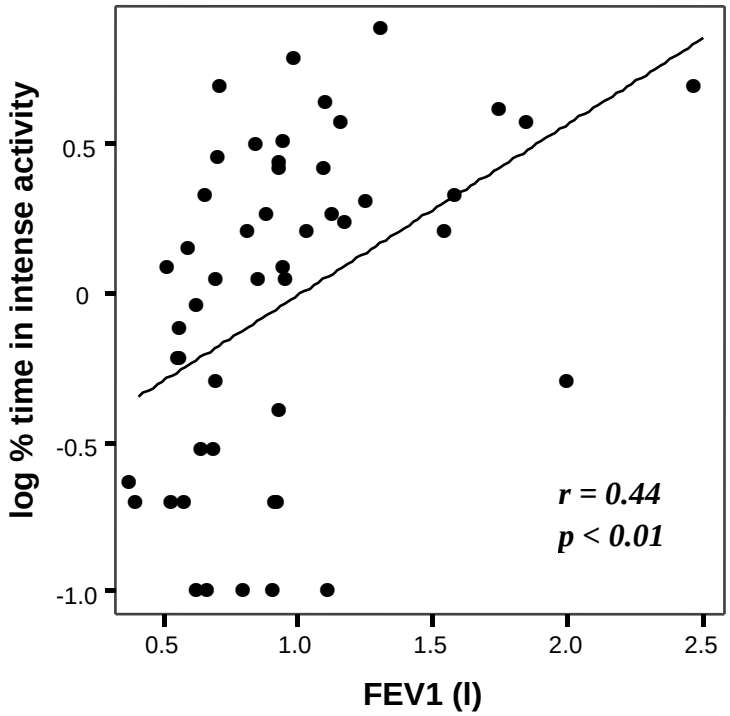


Figure 3.17: Relationship between FEV_1 and log % time intense activity (exacerbators)



3.3.4 Characteristics of exacerbators stratified by degree of physical activity at baseline

To explore differences in the study population in relation to activity the data from the exacerbators were split into tertiles based on the % time active and % time in intense activity. The characteristics of these sub-groups are shown in tables 3.7 and 3.8. Patients who spent less time active tended to have lower FEV_1 absolute and % predicted and also lower FVC. This was also the case with quadriceps force (QF) and 6 minute walk distance. The BODE score was significantly worse in the less active patients, although the MRC score and BMI components did not appear to contribute to this. FEV_1, FVC, QF and BODE (but not the 6MW, BMI or MRC components) and also NEADL score were determinants of intense activity. For both measures of physical activity, the greater differences were generally between the lower and middle tertiles than between the middle and upper tertiles, suggesting that it may be at the extremes of inactivity

that the greatest differences in these variables are seen. In this patient group, age did not appear to predict either baseline % time active or % time in intense activity.

Table 3.7: Subject characteristics (assessment 1, early stages of recovery from exacerbation) by tertiles of % time active

Mean (sd)	Lower Tertile (0.6-4.5% time active) n=20	Middle Tertile (4.7-8.5% time active) n=20	Upper Tertile (8.6-17.7% time active) n=19	p value
Age (years)	69.9 (9.9)	69.6 (8.0)	67.5 (8.9)	NS
FEV_1 (l)	0.7 (0.2)	1.1 (0.5)	1.2 (0.5)	<0.01**
FEV_1 % predicted	37.6 (17.2)	47.2 (18.0)	50.0 (16.9)	<0.01**
FVC (l)	1.7 (0.4)	2.1 (0.8)	2.2 (0.7)	<0.05**
FVC % predicted	64.6 (17.4)	71.2 (19.2)	72.1 (14.9)	NS
BMI	26.1 (8.9)	28.5 (5.4)	30.2 (8.2)	NS
QF (kg)*	17.1 [16.5-20.1]	23.4 [17.2-35.6]	28.8 [24.1-34.0]	<0.05**
6MW (m)	116 (69)	196 (137)	193 (70)	<0.05 $^{\Psi}$
BODE*	8 [7-9]	7 [6-8]	6 [4-7]	<0.05** $^{\Psi}$
$SGRQ_{SYMPTOMS}$	81.5 (15.2)	77.5 (20.8)	79.0 (15.1)	NS
$SGRQ_{ACTIVITY}$	90.2 (7.0)	82.2 (20.2)	85.7 (9.7)	NS
$SGRQ_{IMPACT}$	63.3 (16.7)	60.3 (24.2)	61.0 (19.5)	NS
$SGRQ_{TOTAL}$	74.4 (10.1)	69.8 (20.2)	71.5 (13.4)	NS
MRC*	5 [5-5]	5 [4-5]	4 [4-5]	NS
$HAD_{ANXIETY}$	9.2 (4.0)	8.8 (5.6)	9.0 (5.5)	NS
$HAD_{DEPRESSION}$	9.0 (3.4)	7.2 (4.0)	8.2 (4.8)	NS
LCADL	50.3 (13.0)	44.1 (17.4)	41.6 (13.2)	NS
NEADL	10.3 (5.3)	12.8 (6.0)	13.4 (4.5)	NS

*Median [interquartile range] (not Normally distributed)

** significant between top and lower tertile
$^{\Psi}$ significant between middle and lower tertile
(Bonferroni adjustment for multiple comparisons)

Table 3.8: Subject characteristics (assessment 1, early stages of recovery from exacerbation) by tertiles of % time in intense activity

Mean (sd)	Lower Tertile (0-0.4% time intense movement) n=18	Middle Tertile (0.5-1.8% time intense movement) n=18	Upper Tertile (2.0-7.6% time intense movement) n=17	p value
Age (years)	70.5 (9.6)	70.7 (7.5)	67.1 (9.8)	NS
FEV_1 (l)	0.8 (0.2)	0.9 (0.4)	1.2 (0.5)	<0.01**
FEV_1 % predicted	39.7 (17.2)	42.8 (18.1)	50.1 (17.5)	NS
FVC (l)	1.7 (0.4)	1.8 (0.7)	2.3 (0.7)	<0.05**
FVC % predicted	67.8 (15.0)	65.4 (19.0)	72.8 (16.8)	NS
BMI	26.6 (8.1)	27.7 (6.6)	31.2 (8.2)	NS
QF (kg)*	16.9 [15.7-21.7]	23.7 [18.2-36.3]	26.9 [21.1-33.2]	<0.05**
6MW (m)	130 (80)	162 (114)	194 (86)	NS
BODE*	8 [7-9]	7 [5.5-8]	6.5 [4-8]	<0.01**
$SGRQ_{SYMPTOMS}$	83.7 (14.7)	80.9 (14.6)	79.0 (15.6)	NS
$SGRQ_{ACTIVITY}$	90.5 (6.7)	86.2 (12.0)	85.6 (11.6)	NS
$SGRQ_{IMPACT}$	66.9 (18.7)	60.6 (15.8)	58.2 (24.4)	NS
$SGRQ_{TOTAL}$	76.8 (11.5)	71.7 (11.1)	70.0 (17.5)	NS
MRC*	5 [5-5]	5 [4-5]	5 [4-5]	NS
$HAD_{ANXIETY}$	9.4 (4.2)	8.3 (3.4)	9.1 (6.3)	NS
$HAD_{DEPRESSION}$	8.8 (2.8)	7.1 (3.5)	8.2 (5.2)	NS
LCADL	52.7 (12.5)	41.3 (14.4)	43.2 (14.7)	NS
NEADL	9.2 (5.1)	13.5 (5.4)	13.8 (5.2)	<0.05**

*Median [interquartile range] (not Normally distributed)

** significant between top and lower tertile
(Bonferroni adjustment for multiple comparisons)

3.3.5 Comparison of subjects who stayed in hospital and who received an early discharge

25 patients received an early discharge and thus wore the activity monitor at home. Of these patients, 19 received hospital at home care from the ACTRITE team. 27 patients remained in hospital while wearing the activity monitor. In 8 patients, the monitor reading was commenced as an inpatient, but they were discharged home while still wearing the monitor. They were

excluded from this part of the analysis. There were no readmissions while the subject was still wearing the monitor. Table 3.9 demonstrates the differences between the patients who remained in hospital (IP), and those who received early discharge (H).

Table 3.9: Characteristics of patients (assessment 1, early stages of recovery from exacerbation) who stayed in hospital (IP) or received early discharge (H)

Mean (sd)	IP (n=27)	H (n=25)	p value
Length of Stay (days)*	9 [6-12]	4 [2-6]	<0.01
Age (yrs)	71.1 (9.1)	67.6 (9.1)	NS
FEV_1 (l)	0.9 (0.5)	1.1 (0.4)	NS
FEV_1 % predicted	43.5 (18.0)	45.5 (18.0)	NS
FVC (l)	2.0 (0.9)	2.0 (0.6)	NS
FVC % predicted	71.9 (19.3)	68.1 (16.4)	NS
QF (kg)*	19.8 [16.5-28.6]	21.5 [18.2-30.5]	NS
6MW(m)	158 (118)	183 (92)	NS
$SGRQ_{TOTAL}$	70.2 (16.7)	73.9 (12.4)	NS
MRC*	5 [4-5]	5 [4-5]	NS
London Chest ADL	47.0 (16.4)	43.9 (13.8)	NS
Nottingham Extended ADL	12.6 (5.4)	11.8 (5.5)	NS
% time active*	4.8 [2.4-7.4] [n=26]	8.5 [3.9-12.4] [n=25]	<0.01
% time in intense activity*	0.6 [0.2-2.0] [n=24]	1.6 [0.5-3.8] [n=22]	<0.05

*Median [interquartile range] (not Normally distributed)

Both groups were of similar age with comparable spirometry, quadriceps force and exercise capacity. The median length of stay among subjects who received early discharge was 4 days, in contrast to 9 days for those who did not. For patients who went home with the ACTRITE team, median length of stay was 4 [IQR 2-5] days. Although both groups reported similar health related quality of life and perceptions of ability to carry out activities of daily living, patients who received early discharge demonstrated increased levels of physical activity compared with those who remained in hospital.

3.4 Discussion

In this study we have shown that exacerbators have worse self reported health related quality of life, dyspnoea and impairment of physical activities than a group of stable patients with comparable age and FEV_1. We have also shown that patients who receive an early discharge home are more physically active (spending more time active and in intense activity) than subjects who remain in hospital. Additionally, we have demonstrated the validity of using the Actiwatch (along with the derived thresholds for % time active and intense activity) in this patient group: this reaffirms previous work with the Actiwatch that lower limb activity relates closely to whole body activity(166).

The exacerbators reported significantly worse MRC, SGRQ and LCADL scores than stable patients. It is not clear whether this reflects an exacerbator phenotype of COPD patient, who have worse breathlessness, HRQOL and self reported activity limitation than patients who do not exacerbate, or whether it is the exacerbation itself that temporarily worsens these scores. The MRC score enquires about subjects' current levels of breathlessness while LCADL enquires about breathlessness doing activities in the last few days, which may lead to temporary worsening of these scores in the early stages of exacerbation. SGRQ enquires about symptoms in the last 12 months and 'these days', although again, subjects may reflect on their stable symptoms as being worse when reporting them in the early stages of recovery from an exacerbation.

Although physical activity correlated moderately with airflow obstruction, quadriceps force and exercise capacity in the exacerbators, the correlation of intense activity with 6MW did not reach levels of statistical significance. There was no correlation of physical activity with MRC, SGRQ or LCADL. It appears that, while measuring actual physical activity with accelerometers provides complementary information to that obtained from questionnaires and timed walking tests, these measures should not be used as surrogates for each other.

Patients also demonstrated statistically significant lower levels of physical activity in the early stages of recovery from an exacerbation than stable subjects. Exacerbators spent 94% of the waking day sedentary in contrast to 90% in the stable patients: although statistically significant, it is not known whether the difference is clinically significant and these data highlight the low levels of physical activity in COPD patients as a whole. Patients in the early stages of recovery from exacerbation spent only 1.1% of the day in intense activity such as walking in contrast to 3.7% in stable patients. This equates to exacerbators spending 8 minutes of a 12 hour day walking, in contrast to 27 minutes in stable COPD patients. The exacerbators are a long way off from the 30 minutes of daily moderate physical aerobic activity that is recommended to maintain fitness(12).

This group of exacerbators was of comparable age to those studied by Pitta(77) although Pitta's group had more severe airflow obstruction (median FEV_1 29% predicted versus 40% predicted): however, it is not clear from Pitta's paper whether this measure was post-bronchodilator as with our patients. Despite the more severe airflow obstruction, Pitta's group had better exercise capacity (median 6 minute walk distance 268m versus 137m). Direct comparisons with Pitta's subjects are limited since all patients in that study were hospitalised for at least 10 days while approximately 50% of our subjects received an early discharge, often within 48 hours of the

initial admission. The subjects in our study who wore the DynaPort showed similar levels of activity to those in Pitta's group (median 9.7% of time in weightbearing activities versus 9% in Pitta's group), although the 7 subjects who remained in hospital in this study while wearing the DynaPort were weightbearing for only 4.7% (median) of the time. Median % time walking in Pitta's subjects was 0.7% at day 2 and 1.4% at day 7. This was comparable to the % time in intense activity in our exacerbators (median 1.1% for all subjects, 0.6% for subjects who remained in hospital and 1.6% for subjects who received early discharge to hospital at home). We could not directly compare quadriceps force with Pitta's subjects since a different way of reporting this was employed in their study (torque, expressed as Newton metres). It was surprising that the quadriceps force in our exacerbators was not statistically different from the stable group. This is in contrast to the study by Spruit et al, who found a significantly reduced quadriceps force in 34 hospitalised exacerbators compared with 13 stable COPD patients (of similar age and spirometry to our group)(73). Subjects in our study had a very poor health related quality of life and self reported breathlessness ($SGRQ_{TOTAL}$ mean score = 71.9, MRC median score 5). These parameters were not measured in Pitta's study, but may be a reason why our group of patients demonstrate worse exercise capacity but comparable physical activity to Pitta's less severe (based on spirometry) group. Likewise, our stable patients were less active than a separate stable group of subjects (with similar age and spirometry) that Pitta studied: 3.7% time walking versus 6% in Pitta's subjects and 90.2% time sedentary versus 64% in Pitta's subjects(167). This demonstrates the heterogeneity of COPD and the limitations of extrapolating data from one group of subjects to a wider population.

We were able to identify predictors of impaired physical activity by stratifying activity into tertiles. Both forced expiratory flow and volume, quadriceps force and BODE score were

predictors of % time active and in intense activity. NEADL was a predictor of intense activity and 6 minute walk distance was a predictor of % time active but, surprisingly, not intense activity (the equivalent of walking at a moderate pace), although appropriate trends were demonstrated. The correlation of FEV_1 with physical activity has previously been demonstrated by Walker, who used the Actiwatch on the lower limb of stable COPD patients(166), although the correlation between FEV_1 and walking time using the DynaPort in Pitta's stable patients was very weak(167).

COPD patients demonstrate very low levels of physical activity in the early stages of recovery from an exacerbation. Those who receive an early discharge home are more physically active (spending more time active and in intense activity) than subjects who remain in hospital. We acknowledge that the categorization of patients into the 'early' or 'late' discharge groups was based on whether the activity monitor was worn in hospital or at home, rather than a pre-defined hospital length of stay, and this may therefore have been influenced by other factors, such as how quickly the patient received the initial assessment. Additionally, although the patients who receive early discharge are comparable to those who remain in hospital in terms of age, COPD severity, health status and exercise capacity, there is a degree of selection bias in that certain patients (even though matched in these variables) would be judged not suitable for early discharge. These may be subjects who do not feel well enough to go home yet or hypoxaemic patients who still require hospital oxygen. We cannot therefore conclude from these data that early discharge itself makes patients more active, although it is reasonable to suppose that a patient may do more within the familiarity of their home environment than in the confines of a hospital ward. There is increasing interest in early pulmonary rehabilitation for COPD patients who have recently experienced an exacerbation. This intervention has shown to be of benefit in a

group of exacerbators (with comparable spirometry and SGRQ scores to subjects in this study) who commence PR shortly after discharge(196). It would be worth exploring whether early PR is of benefit in hospitalized patients, who show even greater levels of sedentary behaviour.

A limitation of this study is that the exacerbators in this study did not include the sickest of patients (acidotic patients and those with significant other co morbidity were excluded): moreover, patients who declined participation in the study may have tended to be more frail than subjects who agreed to take part. This may have blunted some of the differences between the stable patients and exacerbators, and may be a reason why the quadriceps force was similar in the two groups. Exercise capacity in the stable patients was assessed by Endurance Shuttle Walk Test, rather than 6MW in the exacerbators: as such, this parameter could not be compared. Another limitation is that we used 2 different instruments to measure physical activity. Although we have validated the DynaPort and Actiwatch against one another and determined thresholds that allow us to derive equivalent data, it would have been preferable to use a single device in all patients.

We have demonstrated that impairment of physical activity occurs across a wide range of COPD subjects in the early stages of exacerbation and that there are features (FEV_1, FVC, quadriceps force and BODE) which help predict subjects whose level of physical activity falls in the lowest tertile. Although we found that FEV_1 is related to physical activity, there are other factors which contribute which cannot be captured by exercise tests or self reported questionnaires, suggesting that measuring physical activity with accelerometers offers additional information about COPD patients.

In this chapter we have demonstrated some of the characteristics of COPD patients in the early stages of recovery from an exacerbation, and have demonstrated that they are less active with worse health related quality of life than comparable stable patients. It is not clear whether this reflects an exacerbator patient phenotype, or whether there is subsequent improvement in these measures in the subsequent few months: this is investigated in Chapter 4.

Chapter 4: Physical activity during recovery from a COPD exacerbation

4.1 Introduction

The primary aims of this part of the study were to examine what happens to the measures of lung function, exercise capacity, quadriceps strength, questionnaire scores and physical activity in the 4 months following the initial exacerbation and evaluate whether re-exacerbation in the follow-up period influences these measures. Secondary aims were to assess whether there was a difference in the degree of recovery between subjects who had received early discharge and those who had remained in hospital for longer after the initial hospitalisation.

4.2 Methods

The methods used have been described in the previous chapter. Although we aimed to assess patients 1 month and 3 months after discharge, re-exacerbations and the general frailty of many of these patients meant that many were unable to attend for assessments 2 and 3 at the pre designated follow up times. The time frames were extended (4 weeks allowed for assessment 2, 8 weeks for assessment 3) in order to include as many subjects as possible in the study. No patients underwent Pulmonary Rehabilitation during this follow up phase.

Table 4.1 illustrates the follow up periods between assessments and the number of patients who completed each assessment pair: in Chapter 3 we explained the reasons for patients withdrawing from the study or being unable to complete an assessment.

Table 4.1: Intervals between assessments for patients following the initial hospitalisation for COPD exacerbation

	Mean (sd) days	Range (days)
Assessment 1- assessment 2 (n=28)	36 (7)	28-55
Assessment 2- assessment 3 (n=26)	73 (16)	54-73
Assessment 1- assessment 3 (n=43)	117 (36)	85-186

4.3 Results

4.3.1 Differences in baseline features of subjects who completed follow up assessments and those who did not

34 patients (57%) withdrew from study or were unable to complete all of the follow up assessments within the allowed time frame. This could introduce bias into the follow up data by the selective withdrawal of sicker patients. Table 4.2 demonstrates the baseline demographics, lung function, quadriceps force, exercise capacity, questionnaire scores and physical activity levels in subjects who completed all 3 assessments and those who did not. There were no significant differences between the two groups, which provided reassurance that subjects who were able to attend all 3 assessments were representative of the study population.

Table 4.2: Baseline characteristics (early stages of recovery from exacerbation) of subjects who completed all assessments (V1,V2 and V3) and those who did not

Mean (sd)	Completed all assessments (n= 26)	Failed to complete all assessments (n=34)	p value
Age (yrs)	69.0 (10.2)	69.2 (7.8)	NS
BMI	29.4 (9.0)	27.4 (6.5)	NS
FEV_1 (l)	1.0 (0.4)	1.0 (0.5)	NS
FEV_1 % predicted	46.1 (18.3)	43.7 (17.5)	NS
FVC (l)	1.9 (0.6)	2.0 (0.8)	NS
FVC % predicted	67.9 (14.5)	70.6 (19.1)	NS
QF (kg)*	22.5 [16.7-32.2]	20.8 [17.1-29.3]	NS
6MW(m)	186 (88)	156 (110)	NS
$SGRQ_{TOTAL}$	71.5 (14.0)	72.2 (15.6)	NS
MRC*	5 [4-5]	5 [4.75-5]	NS
HAD anxiety	7.7 (4.6)	10.0 (5.1)	NS
HAD depression	7.4 (3.7)	8.6 (4.3)	NS
London Chest ADL	42.2 (13.5)	47.4 (15.5)	NS
Nottingham Extended ADL	11.7 (5.5)	12.6 (5.2)	NS
% time active*	6.2 [3.3-10.6]	6 [3.5-11.1]	NS
% time in intense movement*	1.1 [0.2-2.4]	1.3 [0.3-2.7]	NS

*Median [interquartile range]

4.3.2 Changes in variables at follow up assessments

Table 4.3 illustrates the measures of lung function, exercise capacity, quadriceps force, questionnaire scores and physical activity at assessment 1 (early stages of recovery from the initial exacerbation) and the subsequent follow up assessments. Only the data for subjects who attended all 3 assessments are included. Although there were significant improvements between assessments 1 and 2 in FVC, 6MW, AW mean activity score and % time active, this was not the case for post bronchodilator FEV_1, quadriceps force or % time in intense activity. Additionally, the variables that did improve between assessments 1 and 2, subsequently deteriorated so that the

difference between assessments 1 and 3 for any variable was not significant. Questionnaires were not completed at assessment 2, but there was no difference in SGRQ, MRC, HAD, LCADL or NEADL between assessments 1 and 3.

Table 4.3: Measures recorded at each assessment [1: early stages of recovery from initial hospitalisation, 2: 1-2 months after assessment 1, 3: 3-5 months after assessment 1] (n=26)

Mean (sd)	Assessment 1	Assessment 2	Assessment 3	p value
FEV_1 (l)	1.1 (0.4)	1.2 (0.5)	1.1 (0.5)	NS
FEV_1 % predicted	47.3 (18.4)	50.8 (19.5)	49.4 (18.7)	NS
FVC (l)	2.0 (0.6)	2.2 (0.7)	2.1 (0.7)	<0.05**
FVC % predicted	67.6 (14.6)	73.2 (21.1)	69.1 (19.5)	NS
QF (kg)*	23.7 [18.7-32.3]	22.5 [20.4-34.9]	23.5 [19.1-33.3]	NS
6 MW (m)	196.3 (88.5)	231.0 (85.4)	206.2 (86.3)	<0.05**
AW mean activity [n=20]*	28.8 [14.2-42.9]	41.8 [23.7-62.8]	37.7 [27.4-48.2]	<0.05**
% time active*	6.2 [3.1-10.5]	8.2 [5.4-12.9]	6.6 [5.3-10.1]	<0.05**
% time in intense activity*	0.6 [0.2-1.7]	1.5 [0.6-2.3]	1.0 [0.6-1.9]	NS
$SGRQ_{SYMPTOMS}$	79.0 (15.6)		80.6 (13.0)	NS
$SGRQ_{ACTIVITY}$	86.8 (9.5)		88.5 (11.0)	NS
$SGRQ_{IMPACT}$	60.4 (20.9)		56.0 (20.6)	NS
$SGRQ_{TOTAL}$	71.5 (14.0)		69.9 (15.1)	NS
MRC*	5 [4-5]		5 [4-5]	NS
$HAD_{ANXIETY}$	7.7 (4.5)		8.6 (4.5)	NS
$HAD_{DEPRESSION}$	7.4 (3.7)		8.2 (2.9)	NS
London Chest ADL	41.8 (13.8)		41.5 (14.7)	NS
Nottingham Extended ADL	11.4 (5.5)		11.3 (5.2)	NS

*Median [interquartile range]

* *significant between V1 and V2
(Bonferroni adjustment for multiple comparisons)

Figures 4.1-4.4 illustrate the changes between assessments for individual subjects who completed all 3 assessments. Although there is considerable variation between patients, the patterns suggested in table 4.3 can be seen, with a trend towards improvement in 6MW, % time active and % time in intense activity between assessments 1 and 2, which subsequently declines at assessment 3, with no significant change in quadriceps force across the assessments. Of the

subjects who completed all 3 assessments, 78% improved % time active and 68% improved % time in intense activity between assessments 1 and 2, whereas only 44% improved % time active and 39% improved % time in intense activity between assessments 2 and 3. Of the subjects who completed assessments 1 and 3, 42% failed to show improvement in either % time active or % time in intense activity between the assessments (Table 4.4).

Figure 4.1: Measures of 6 minute walk distance at each assessment

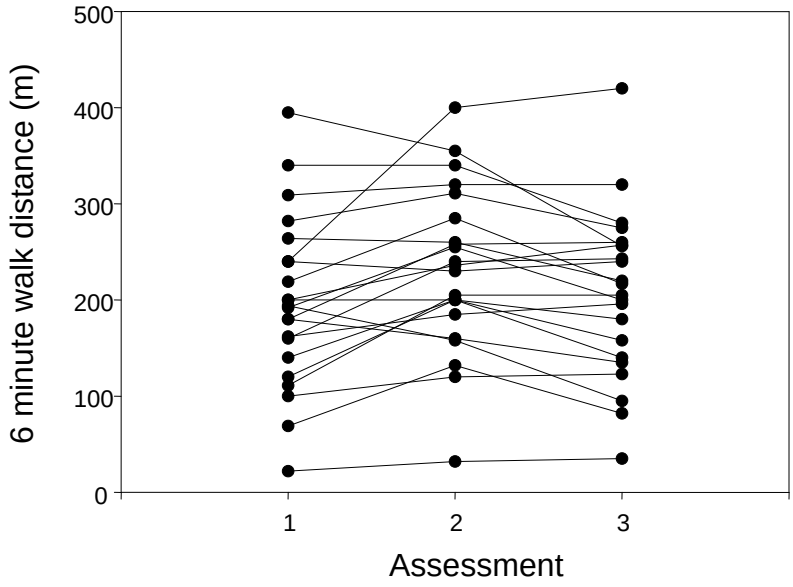


Figure 4.2: Measures of quadriceps force at each assessment

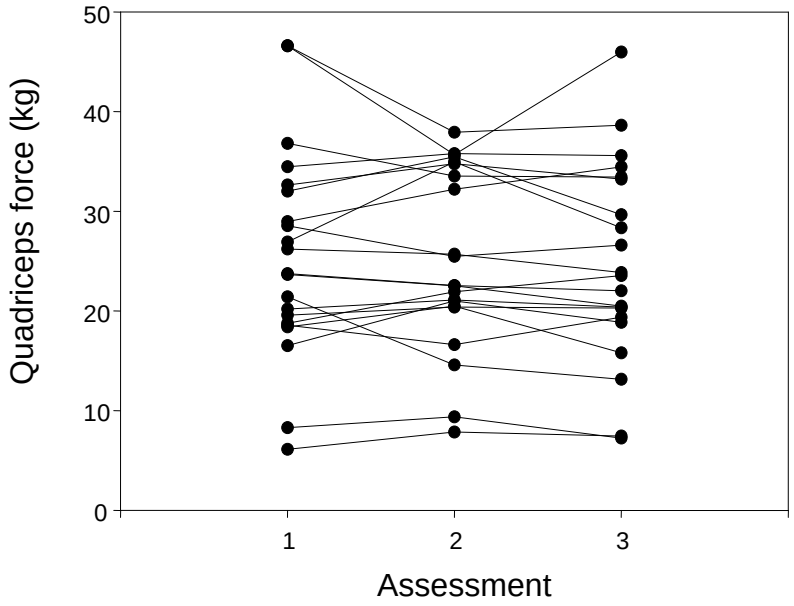


Figure 4.3: Measures of % time active at each assessment

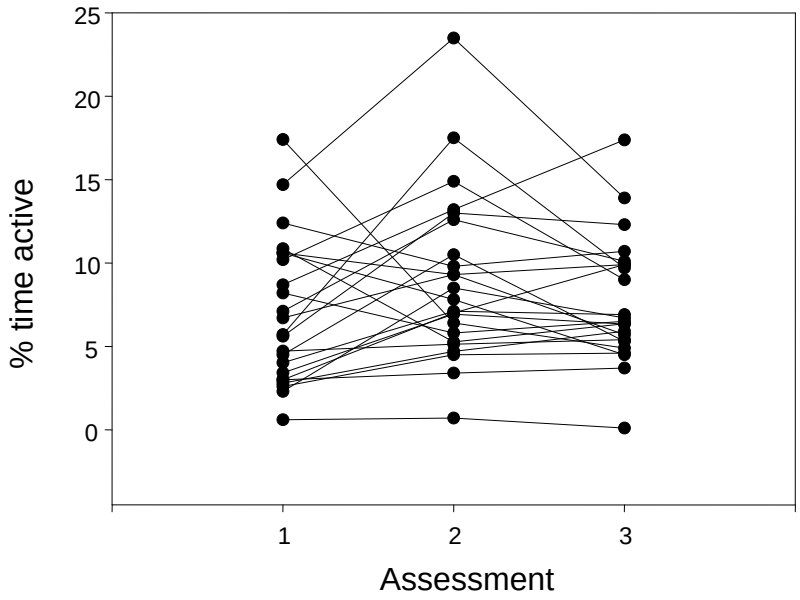


Figure 4.4: Measures of % time in intense activity at each assessment

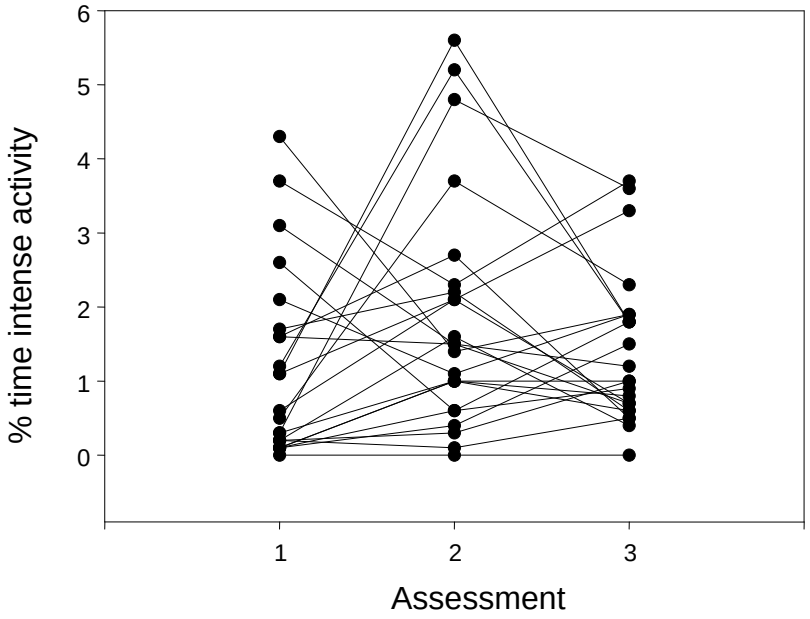


Table 4.4: Number of patients improving physical activity or not between assessments

		% time active	% time in intense activity
V1-V2	Number improving	21 (78%)	17 (68%)
	Number not improving	6 (22%)	8 (32%)
	Unknown	*33*	*35*
V2-V3	Number improving	11 (44%)	9 (39%)
	Number not improving	14 (56%)	14 (61%)
	Unknown	*35*	*37*
V1-V3	Number improving	25 (58%)	25 (58%)
	Number not improving	18 (42%)	18 (42%)
	Unknown	*17*	*17*

In figures 4.3 and 4.4, it appears that a number of subjects who show the largest increases in activity from assessment 1 to assessment 2, subsequently show the largest falls from assessment 2 to assessment 3. There is a negative correlation between change in physical activity from assessments 1 to 2, and assessments 2 to 3 ($r = -0.54$, $p < 0.01$ for % time active; $r = -0.70$, $p < 0.01$ for % time in intense activity) [figures 4.5 and 4.6].

Figure 4.5: Change in % time active for assessment 2-3 relative to assessment 1-2

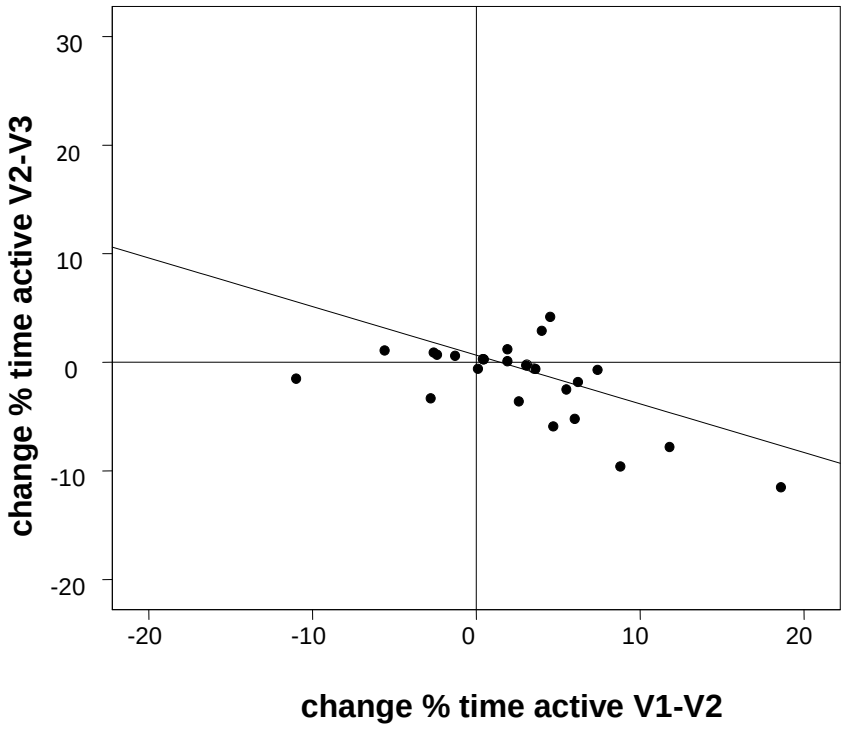
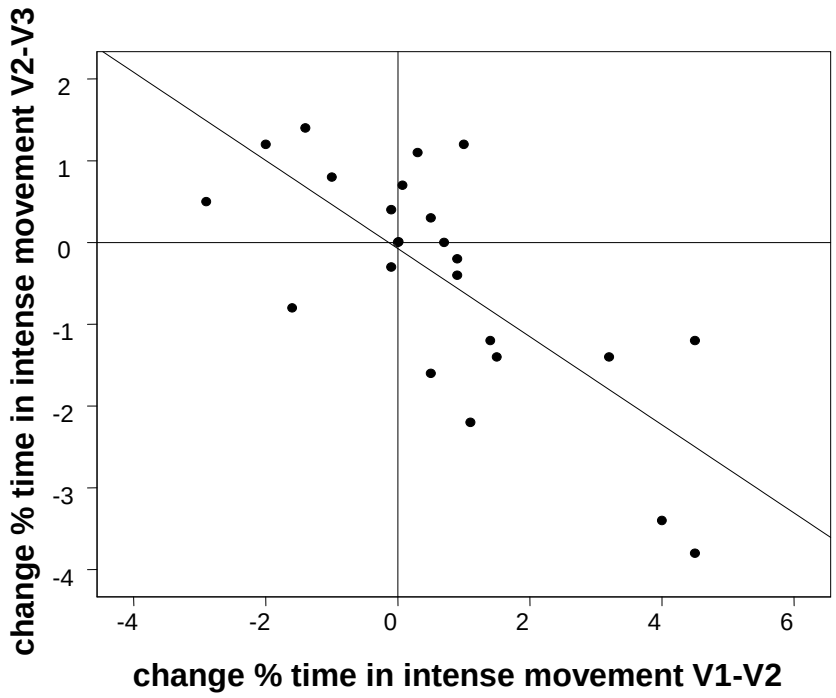


Figure 4.6: Change in % time in intense movement for assessment 2-3 relative to assessment 1-2



4.3.3 Exacerbations in the follow up period and relationship to baseline physical activity

Table 4.5 demonstrates the mean number of readmissions for COPD exacerbation, further courses of oral corticosteroids and further courses of antibiotics (for a COPD exacerbation) during the follow up period. This information was obtained from medical records and patient report. 36 patients received at least one additional course of oral corticosteroids, 41 patients received at least one additional course of antibiotics and 24 patients had at least one further readmission for a separate COPD exacerbation during the follow up period.

Table 4.5: Events (further prednisolone, antibiotics or readmission) over the 4 month course of follow up following initial hospitalisation

	Mean number	No. subjects with zero	No. Subjects with ≥1	No. Subjects in whom data unknown
Further Prednisolone	1.8 (1.9)	15	38	7
Further Antibiotics	2.1 (1.8)	10	43	7
Readmission	0.8 (1.0)	29	24	7

Table 4.6 demonstrates baseline physical activity (assessment 1) in relation to exacerbations during the 4 month follow up period between assessments 1 and 3. Patients who had one or more further exacerbation (requiring further antibiotics or prednisolone or both) spent significantly less time active and in intense activity at baseline than patients who did not, while patients who were readmitted for exacerbation spent significantly less time active at baseline than patients who were not. $SGRQ_{TOTAL}$ at baseline was also a predictor of re admission and re exacerbation in the 4 month follow up period.

Table 4.6: Levels of physical activity and $SGRQ_{TOTAL}$ at baseline (early stages of recovery from exacerbation) in subjects who had further exacerbation or readmission between assessments 1 and 3 (3-5 months later)

	N	Median [IQR] % time active	p value	N	Median [IQR] % time in intense activity	p value	N	Mean (sd) $SGRQ_{TOTAL}$ at baseline	p value
no exacerbation	9	10.6 [6.8-12.4]	<0.05	8	2.7 [2.2-3.6]	<0.05	9	61.2 (17.2)	<0.05
exacerbation	43	5.5 [3.0-9.0]		41	0.7 [0.2-1.8]		44	75.3 (11.4)	
no readmission	29	7.5 [3.8-10.8]	<0.05	27	1.6 [0.2-3.1]	NS	29	69.1 (14.4)	<0.05
readmission	24	5.2 [3.1-6.5]		23	0.6 [0.2-1.8]		24	76.9 (11.5)	

4.3.4 Exacerbations in the follow up period and influence on changes in physical activity

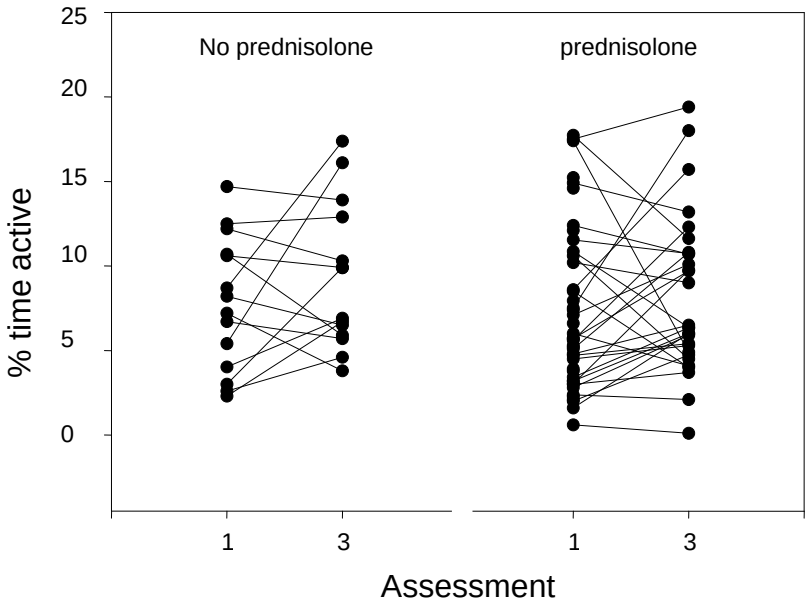
The mean changes in activity between those who experienced further exacerbations and those who did not is shown in table 4.7. There were no significant differences in change of % time active or % time in intense activity between patients who either received further prednisolone, further antibiotics or readmission, and those who did not.

Table 4.7: mean changes in activity in subjects who received or did not receive further prednisolone/antibiotics/readmission between assessments 1 and 3

	N	Mean (sd) change % time active V1-V3	p value	N	Mean (sd) change % time in intense activity V1-V3	p value
no prednisolone	15	3.5 (8.7)	NS	14	0.2 (1.2)	NS
prednisolone	29	0.8 (4.8)		29	0.4 (1.6)	
no antibiotics	10	3.9 (10.5)	NS	9	-0.1 (1.5)	NS
antibiotics	34	1.1 (4.6)		34	0.4 (1.5)	
no readmission	27	1.7 (7.7)	NS	26	0.1 (1.6)	NS
readmission	17	1.7 (3.5)		17	0.6 (1.2)	

Figures 4.7-4.9 illustrate the changes in physical activity in individuals who received treatment or readmission for a further exacerbation versus those who did not between assessments 1 and 3.

Figure 4.7: Changes in physical activity (% time active and in physical activity) in patients who had no further prednisolone or ≥1 courses between assessments 1 and 3



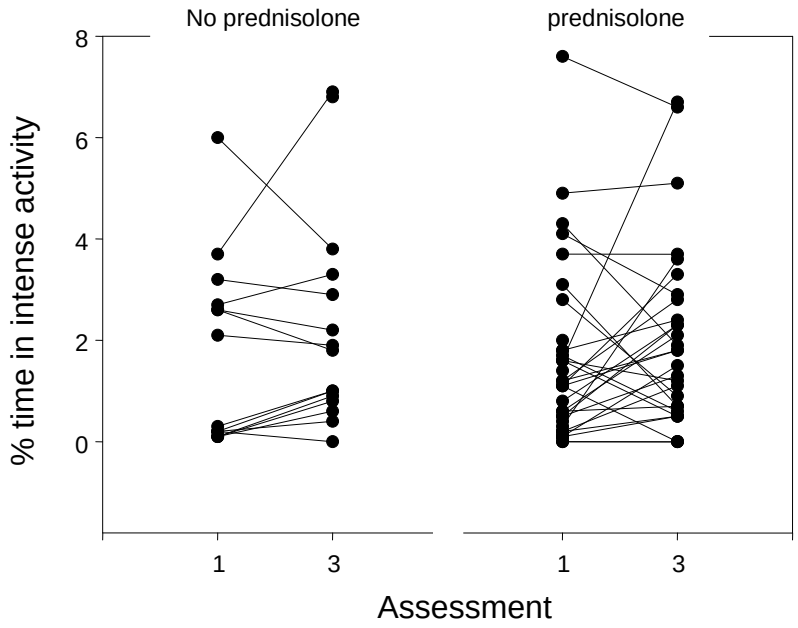
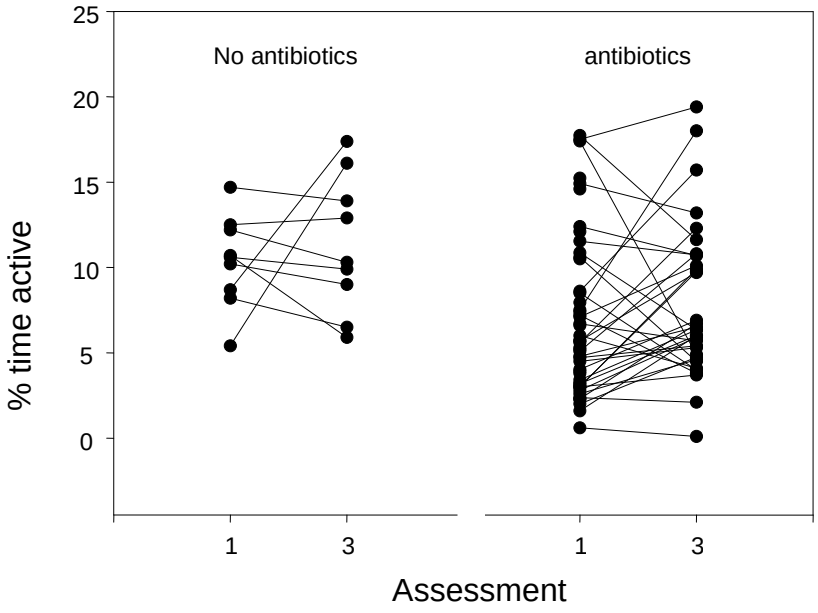


Figure 4.8: Changes in physical activity (% time active and in physical activity) in patients who had no further antibiotics or ≥1 courses between assessments 1 and 3



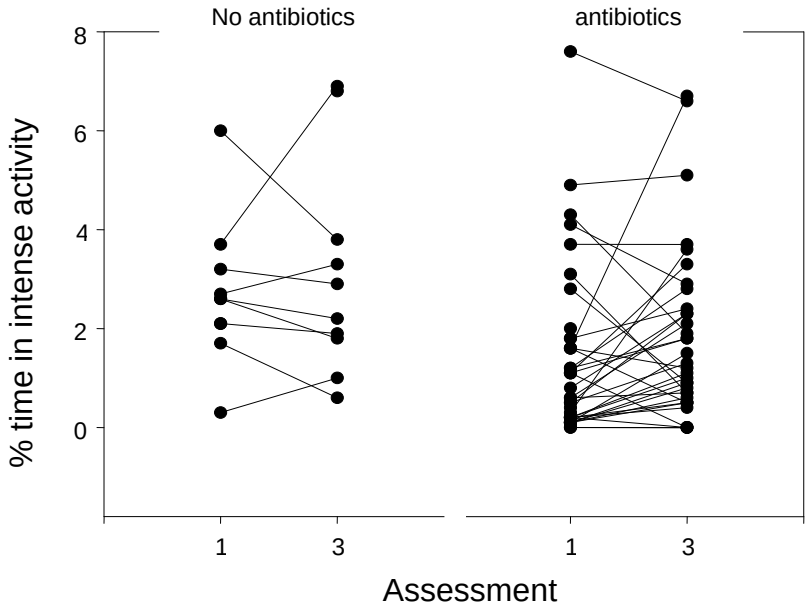
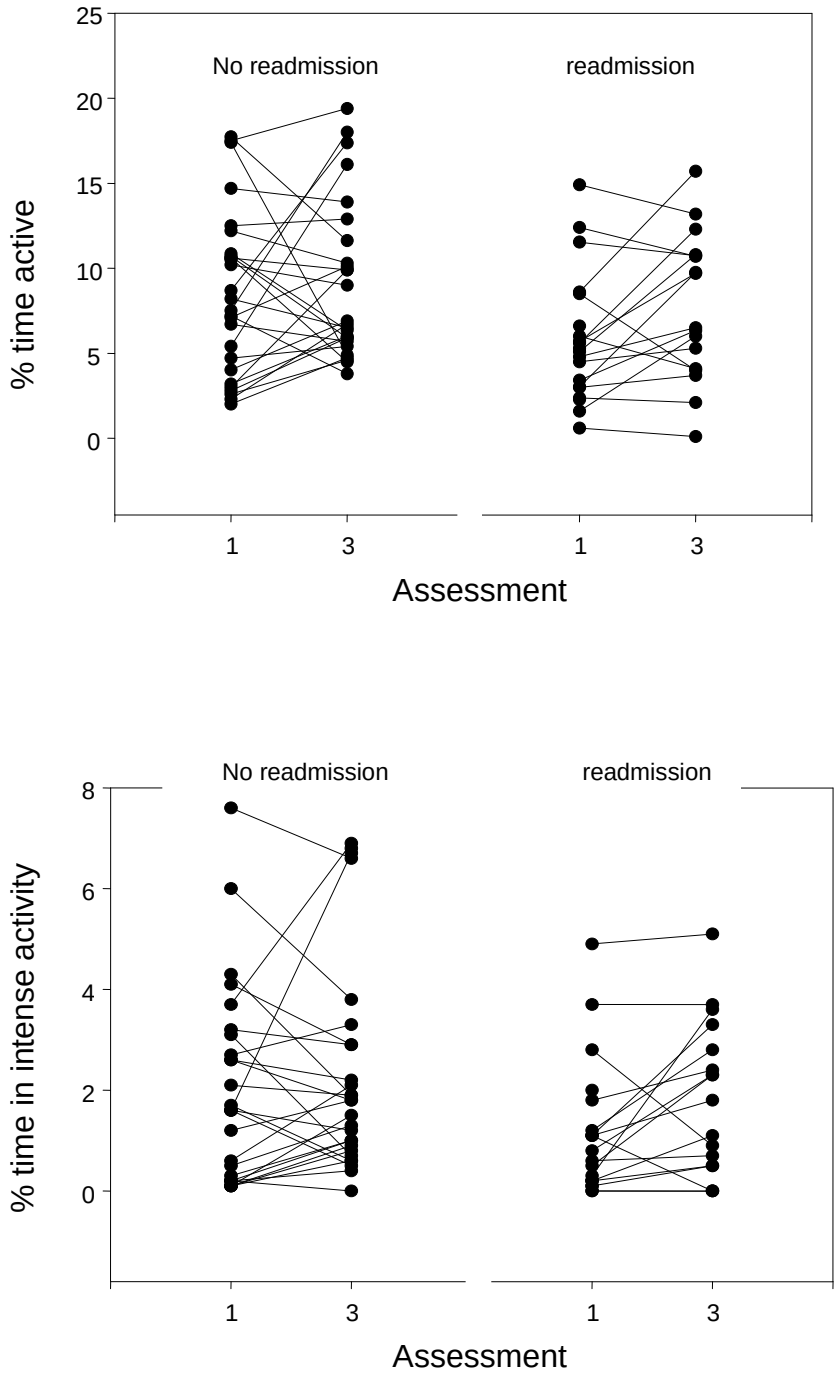


Figure 4.9: Changes in physical activity (% time active and in physical activity) in patients who had no readmissions or ≥1 readmission for COPD exacerbation between assessments 1 and 3



Although further exacerbation or readmission did not impact on the change in physical activity between assessments 1 and 3, they did have more of an impact on health related quality of life. Patients who did not receive any further antibiotics or prednisolone showed a clinically significant improvement (fall of >4) in $SGRQ_{TOTAL}$, while patients who did re exacerbate showed no change in this measure between assessments. Subjects who did not have further exacerbations had lower $SGRQ_{TOTAL}$ scores to start with (Table 4.6). There was also a statistically significant difference in SGRQ improvement between subjects who did or did not receive further antibiotics (Table 4.8).

Table 4.8: mean changes in $SGRQ_{TOTAL}$ in subjects who received or did not receive further prednisolone/antibiotics/readmission between assessments 1 and 3

	N	Mean (sd) change SGRQ V1-V3	p value
no prednisolone	14	-4.3 (6.3)	NS
prednisolone	29	-0.2 (8.5)	
no antibiotics	10	-6.4 (6.2)	<0.05
antibiotics	33	0.0 (8.0)	
no readmission	26	-2.8 (8.3)	NS
readmission	17	0.4 (7.5)	

4.3.5 Changes in Physical Activity in individuals who had received early discharge compared with those who did not

As demonstrated in Chapter 3, exacerbators who received early home discharge (H) spent significantly more time active and in intense activity than patients who remained in hospital (IP). However, levels of physical activity at assessment 2 and assessment 3 were not significantly different between the 2 groups (Table 4.9).

Although there appeared to be a trend towards larger improvements in % time active at assessment 2 and 3 in the IP group, this did not reach levels of statistical significance. There

were no significant differences in the change of % time in intense activity between the IP and H patients (Table 4.10).

Table 4.9: Comparison of physical activity levels at assessment 1, 2 and 3 in subjects who had received early discharge (H) and those who remained in hospital following the initial admission (IP)

Median [IQR]	IP		H		p value
V1 % time active	4.8 [2.4-7.4]	[n=26]	8.5 [3.9-12.4]	[n=25]	<0.01
V1 % time in intense activity	0.6 [0.2-2.0]	[n=24]	1.6 [0.5-3.8]	[n=22]	<0.05
V2 % time active	7.2 [5.1-10.3]	[n=8]	7.0 [5.0-12.8]	[n=13]	NS
V2 % time in intense activity	1.3 [0.4-2.3]	[n=8]	1.6 [0.7-3.5]	[n=12]	NS
V3 % time active	6.3 [4.9-10.5]	[n=16]	10.1 [4.8-13.0]	[n=21]	NS
V3 % time in intense activity	1.2 [0.6-2.6]	[n=17]	2.3 [0.8-4.5]	[n=21]	NS

Table 4.10: Changes in physical activity (absolute and %) relative to first assessment in exacerbators who had received early discharge (H) and those who remained in hospital (IP)

Mean (sd)	IP		H		p value
Absolute change V1-V2 % time active	3.5 (7.0)	n=8	1.6 (5.6)	n=12	NS
% change V1-V2 % time active	79.5 (113.4)		47.8 (66.2)		NS
Absolute change V1-V3 % time active	4.1 (7.7)	n=17	0.3 (5.6)	n=20	NS
% change V1-V3 % time active	120.2 (213.6)		29.5 (80.3)		NS
Absolute change V1-V2 % time in intense activity	0.7 (2.0)	n=8	0.7 (2.0)	n=10	NS
% change V1-V2 % time in intense activity	236.6 (524.7)		273.5 (323.7)		NS
Absolute change V1-V3 % time in intense activity	0.6 (1.0)	n=17	0.2 (2.0)	n=19	NS
% change V1-V3 % time in intense activity	185.4 (286.8)		173.4 (379.4)		NS

4.4 Discussion

We have studied a group of patients who were hospitalised with a COPD exacerbation and have investigated what happens to exercise capacity, health related quality of life, functional status and objectively measured levels of physical activity over a 4 month period after the initial hospitalisation. These data suggest that there is an overall improvement in exercise capacity and physical activity in the 5 weeks following the initial hospitalisation; this is comparable with the increased walking time identified in Pitta's patients one month after discharge for exacerbation(77). However, our data suggest that exercise capacity and physical activity subsequently decline in the following 11 weeks towards levels in the early stages of recovery from the initial exacerbation. In this patient group, quadriceps force appears to be static across the 3 assessments. This is in contrast to Spruit's study which showed significant improvements in quadriceps strength between day 8 of hospitalisation for a COPD exacerbation and 90 days after discharge in a group of patients with similar age and spirometry to this study(73), although our findings of static quadriceps force and exercise capacity are consistent with Seymour's control group at 3 months in a study of early pulmonary rehabilitation(197).

Previous work has been carried out to investigate the time course of recovery from a COPD exacerbation. Seemungal et al followed up 101 patients by means of peak flow readings and diary cards of symptoms. Following an exacerbation (the majority of which were treated in the community), median recovery times were 6 days for peak flow and 7 days for symptom score, although full recovery of peak flow and symptoms at 35 days had not occurred in 24.8% and 13.9% of subjects respectively(38). Our work suggests that 1 months' follow up may not give the full picture and that the effects of an exacerbation may be longer lasting.

The peak levels of physical activity across the 3 assessments occur at assessment 2: at this stage, % time active (8.2 [IQR 5.4-12.9]) is comparable to the 37 stable patients studied in the previous chapter (9.8 [IQR 5.8-14.7]) although % time in intense activity is lower in this group (1.5 [IQR 0.6-2.3] vs 3.7 [IQR 2.0-5.7]). We do not know whether these exacerbators have a lower baseline level of physical activity, or whether the exacerbation with which they entered the study caused a drop in intense activity such as walking that never recovers to pre-exacerbation levels. A prospective study that follows up stable patients and tracks them through subsequent exacerbations would be necessary to answer this question. Levels of physical activity in the early stages of recovery from exacerbation predicted re exacerbation and readmission in the subsequent 4 months: % time in intense activity was the predictor of re exacerbation, and % time active predicted both re exacerbation and readmission. This is consistent with Garcia-Aymerich's study, in which a high level of self reported physical activity among 340 patients who had been hospitalised for a COPD exacerbation was associated with a 46% reduction in the risk of COPD readmission over a mean follow up of 1.1 years(43). Pitta's study looked at objectively recorded physical activity using the DynaPort in hospitalised COPD patients and found that patients who were readmitted with a further exacerbation within 12 months showed lower walking time 1 month after the initial exacerbation than patients who were not readmitted: however, there were only 6 patients in the latter group, amongst whom high walking time in 2 subjects appears to have created the significant difference(77).

In this study, although there was considerable variation from patient to patient, 42% of subjects failed to demonstrate improved physical activity from the early stages of recovery from a COPD exacerbation to assessment in a stable phase 4 months later. Moreover, there were no significant changes in health related quality of life scores (except for the minority of patients who had no

further exacerbation) or self assessed functional impairment over this time period. This is in contrast to a study by Spencer et al which showed significant improvement in SGRQ and its domains over the subsequent 26 weeks following a COPD exacerbation in 438 COPD patients(37). However, the subjects in Spencer's study were younger with better baseline SGRQ scores and the majority were not hospitalised in comparison to this patient group. Patients in our study who did not experience further exacerbations or readmissions had a better baseline $SGRQ_{TOTAL}$ and this subsequently improved further 4 months later. However, the majority of subjects did re exacerbate, leading to no collective change in $SGRQ_{TOTAL}$ over the follow up period.

Limitations in these data are the small number of patients who managed all 3 assessments. A further limitation is that limited availability of monitors meant that it was not always possible for subjects to wear the same activity monitor at each assessment. This may have affected the variability in individual data from assessment to assessment, but it will not have affected the measures of group data. The data for assessment 1 was obtained 4-6 days since the initial admission. Patients may have recovered (at least partially) by the time this assessment was carried out. This may explain the limited or lack of improvement in lung function, exercise capacity and peripheral muscle strength between these assessments.

The negative correlation between change in physical activity between assessments 1-2, and assessments 2-3 may be a physiological phenomenon, where those who showed the greatest improvement from assessment 1 to assessment 2 exhausted themselves and subsequently declined from assessment 2 to 3, or it may reflect regression to the mean.

Exacerbators who received early home discharge (H) spent significantly more time moving and in intense activity in the early stages of recovery than patients who remained in hospital (IP). However, the IP group appeared to 'catch up' with the H group over the subsequent few months. This would suggest that early discharge itself is associated with increased activity rather than that patients who are intrinsically more active are the ones who receive the earlier discharge. This lends weight to the concept that hospitalised patients have the capacity to carry out more physical activity and inpatient early pulmonary rehabilitation is a therapy worth further exploration.

The high baseline health related quality of life scores which do not improve after the exacerbation, and the failure of these patients to improve quadriceps strength or sustain improvement in exercise capacity or physical activity (whether further exacerbations occurred or not) suggests that we have studied a particularly sick and frail COPD population. Although these were not particularly sick patients in physiological terms (mean FEV_1 45% predicted and patients with significant comorbidities or acidotic respiratory failure being excluded), the high SGRQ, MRC and LCADL scores would suggest that these patients are markedly affected by respiratory symptoms, experience high levels of breathlessness and have marked functional limitation. These patients' poor health is also demonstrated by the fact that 80% suffered at least one further exacerbation and 45% were readmitted for exacerbation in the following 4 months. This patient group may have 'bottomed out' either at or before the exacerbation with which they entered the study, leaving them with little reserve to sustain improved levels of physical activity once the exacerbation resolved.

It appears that this group of patients does not demonstrate sustained improvements in exercise capacity, peripheral muscle strength or health related quality of life in the 4 months following

hospitalisation for COPD exacerbation, in contrast to previous studies. Moreover, we have shown that these patients demonstrate only a transient improvement in physical activity after the initial hospitalisation. We do not know what the levels of physical activity were before the initial exacerbation, so we do not know from this study if the initial hospitalisation resulted in a change in physical activity levels, although it is reasonable to expect that this may be the case: Donaldson has previously shown that exacerbations correlate with increased time spent indoors(39). We have demonstrated that there are no significant changes in physical activity between the early stages of exacerbation and 4 months later, regardless of whether patients re exacerbate or are readmitted. We appear to have identified a particularly sick group of COPD patients who show little recovery from the initial hospitalisation. There is evidence that pulmonary rehabilitation delivered after hospitalisation improves readmissions and health related quality of life(196, 197). Whether such a therapy would have an impact on this patient group is not clear. So far we have investigated these patients within a 4 month time window following the exacerbation. Chapter 5 examines characteristics in the 12 months preceding and following the hospitalisation.

Chapter 5: Predictors of readmission and mortality at 12 months

5.1 Introduction

In Chapter 4, we reported that levels of physical activity in the early stages of recovery from exacerbation predicted re exacerbation and readmission in the subsequent 4 months. In this chapter our primary aim was to investigate whether baseline health status, exercise capacity, physical activity or length of initial admission predicted readmission or death in the following 12 months. Secondary aims were to assess the relationships between these variables and admissions in the previous 12 months.

5.2 Methods

Using the hospital database we accessed data on COPD related admissions in the 12 months before and after the baseline admission (and also the cause for the readmission using the WHO ICD-10 classification) for the 60 patients in the study. Admissions for acute bronchitis (J20), COPD exacerbation (infective and non infective, J44), lower respiratory tract infection (J22), respiratory failure (J96) and pneumonia (J18) were included as a COPD related admission. We also identified which patients were alive or dead 12 months later, and the cause of death.

5.3 Results

5.3.1 Admisions prior to baseline visit and readmissions and mortality in the following 12 months

10 patients died in the 12 months following the initial assessment and 50 survived. 6 patients died from respiratory related causes (pneumonia, respiratory failure, COPD exacerbation), 1

died from myocardial infarction and 1 died from peritonitis and colitis: we were unable to ascertain the cause of death for 2 patients.

Analysis of data at the initial assessment relating to hospital admissions in the previous 12 months was carried out on all 60 patients. However, analysis of data relating to readmissions over the following 12 months was carried out only on the 50 patients who were still alive at 12 months, so that a full 12 months readmission data was available for every patient. 37/60 patients had received at least 1 admission in the previous 12 months and 34/50 patients received at least 1 further admission in the following 12 months (Table 5.1). The number of admissions in the preceding 12 months did not correlate with the number of readmissions in the following 12 months ($R=0.24$, $p>0.05$, figure 5.1). Similarly, whether or not there had been ≥1 admission in the previous 12 months was not related to whether or not there was ≥1 readmission in the next 12 months ($\chi^2=3.33$, $p>0.05$, Table 5.2.)

Table 5.1: number of COPD related admissions in the preceding 12 months and the following 12 months after the first study assessment

		Patients alive at 12 months (N=50)	All patients (N=60)
Admissions (COPD related) in previous 12 months	Mean (sd) number admissions	1.6 (1.8)	1.7 (1.7)
	No. with 0 admissions	19	23
	No. with 1 admission	10	10
	No. with ≥2 admissions	21	27
Readmissions (COPD related) in following 12 months	Mean (sd) number readmissions	1.7 (2.0)	1.8 (2.0)
	No. with 0 readmissions	16	17
	No. with 1 readmission	15	19
	No. with ≥2 readmissions	19	24

Figure 5.1: Relationship between number of COPD related admissions in the preceding 12 months and following 12 months after the first study assessment in 50 subjects still alive at 12 months

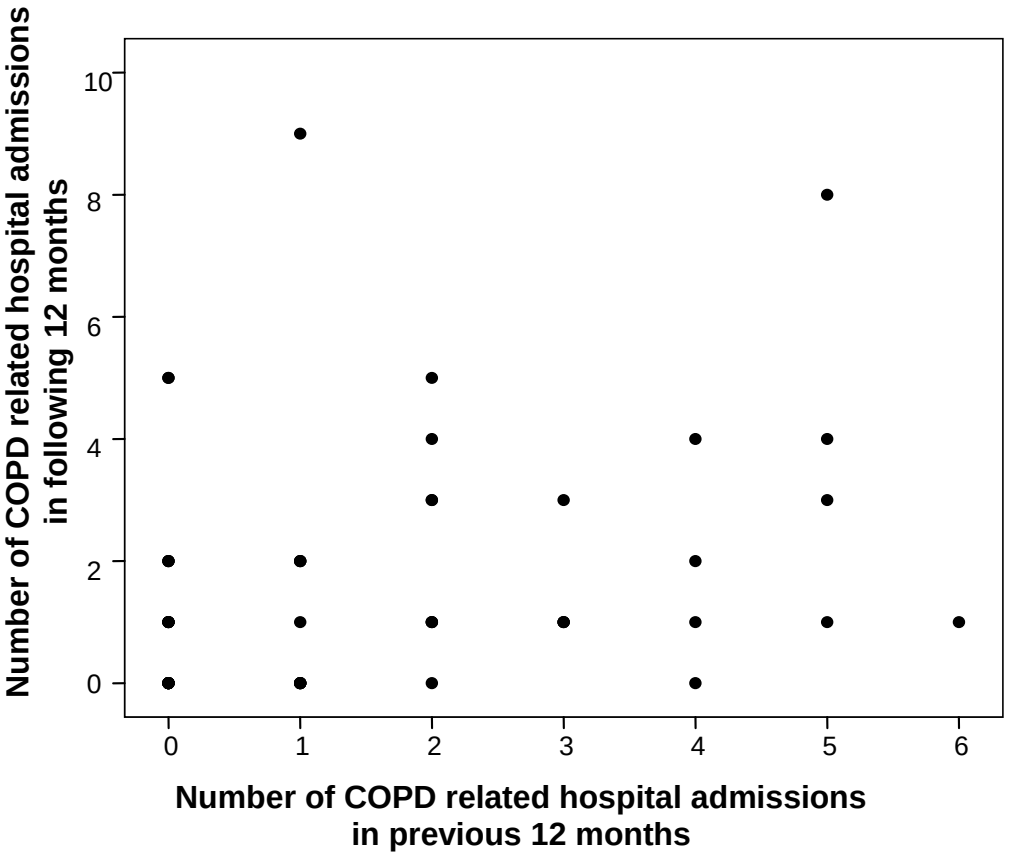


Table 5.2: ≥1 admission in the previous 12 months and ≥1 readmission in the next 12 months tabulation in 50 subjects still alive at 12 months

		≥1 readmission at 12 months		
	TOTAL	Yes	No	
Admission past 12 months	31	24	7	$\chi^2 = 3.326$
No admission past 12 months	19	10	9	NS
TOTAL	50	34	16	

5.3.2 Predictors of mortality at 12 months

Table 5.3 compares the baseline characteristics (assessment 1, day 4-6 since admission for the initial exacerbation) of the 10 patients who had died at 12 months and the 50 patients who were still alive. The BODE score as well as its FEV_1 component predicted mortality, although the BMI, MRC and 6MW components of BODE did not. FEV_1 % predicted and FVC % predicted were also predictors of mortality at 12 months. Neither quadriceps force, SGRQ, or physical activity (assessed by questionnaire or accelerometer) predicted 12 month mortality.

Table 5.3: Baseline characteristics (assessment 1) of patients dead and alive 12 months after assessment 1

Mean (sd)	Alive at 12 mths [n=50]	Dead at 12 mths [n=10]	p value
Age (yrs)	69.0 (9.1)	69.5 (8.0)	NS
BMI	28.8 (8.0)	25.4 (4.6)	NS
FEV_1 (l)	1.0 (0.5)	0.8 (0.2)	<0.05
FEV_1 % predicted	47.3 (18.0)	31.9 (8.7)	<0.01
FVC (l)	2.0 (0.7)	1.8 (0.4)	NS
FVC % predicted	72.0 (17.3)	56.7 (8.9)	<0.01
6MW(m)	168 (101)	170 (110)	NS
$SGRQ_{TOTAL}$	71.2 (15.6)	75.2 (10.3)	NS
MRC*	5 [4-5]	5 [5-5]	NS
BODE score*	7.0 [5.5-8.0]	8.0 [6.5-9.0]	<0.05
QF (kg)*	21.5 [17.0-28.5]	26.1 [17.5-35.7]	NS
QF/BMI % ratio**	88 (40)	104 (42)	NS
HADanxiety	9.2 (5.2)	7.8 (3.2)	NS
HADdepression	7.8 (4.2)	9.4 (3.3)	NS
London Chest ADL	44.8 (15.3)	46.9 (12.7)	NS
Nottingham Extended ADL	12.5 (5.2)	12.6 (5.4)	NS
% time active*	6.7 [3.5-10.8] [n=49]	5.7 [2.5-8.2] [n=10]	NS
% time in intense activity*	1.2 [0.2-2.7] [n=44]	0.6 [0-1.7] [n=9]	NS

*Median [interquartile range]

**QF/BMI ratio < 120% is considered weak(76)

5.3.2.1 Multivariate analysis

Stepwise binary logistic regression analysis was performed, with mortality at 12 months as the dependent, and age, FEV_1, FEV_1 % predicted, FVC, FVC % predicted, quadriceps force, 6MW, BODE, $SGRQ_{TOTAL}$, MRC, HADa, HADd, LCADL, % time active and % time in intense activity as covariates. Only FVC % predicted was a significant independent predictor of mortality at 12 months (Table 5.4).

Table 5.4: Multivariate analysis output for predictors of mortality 12 months after assessment 1: FVC was the only predictor of mortality at 12 months

	B	S.E.	Sig.	Exp(B)	95.0% C.I.	
					Lower	Upper
FVC % predicted	-.054	.027	.048	0.948	.898	.999
Constant	1.749	1.673	.296	5.749		

5.3.2.2 Kaplan Meier plots of survival at 12 months

Figures 5.2-5.6 are Kaplan Meier plots of 12 month survival according to whether the measured parameter was less than or greater than/equal to the median reading. There were significant differences between patients stratified by FEV_1 and FEV_1 % predicted. There was a non-significant trend with respect to MRC score. In terms of physical activity, there was no difference in survival when patients were stratified by either % time active or % time in intense activity.

Figure 5.2: Kaplan-Meier plot of 12 month survival according to FEV_1

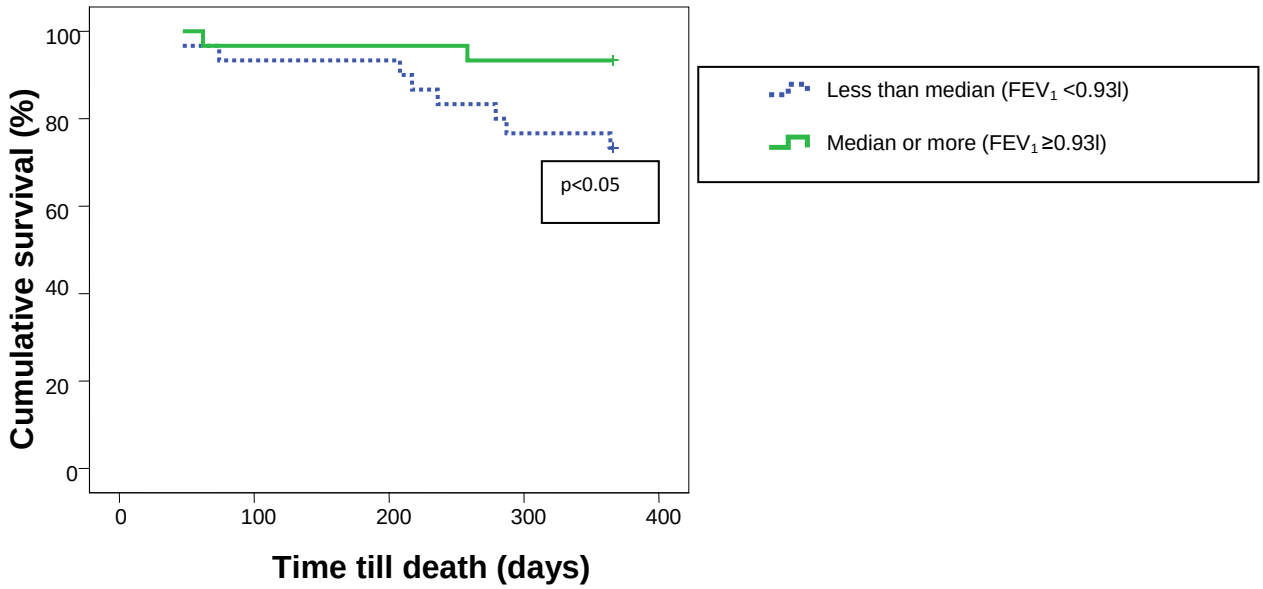


Figure 5.3: Kaplan-Meier plot of 12 month survival according to FEV_1 % predicted

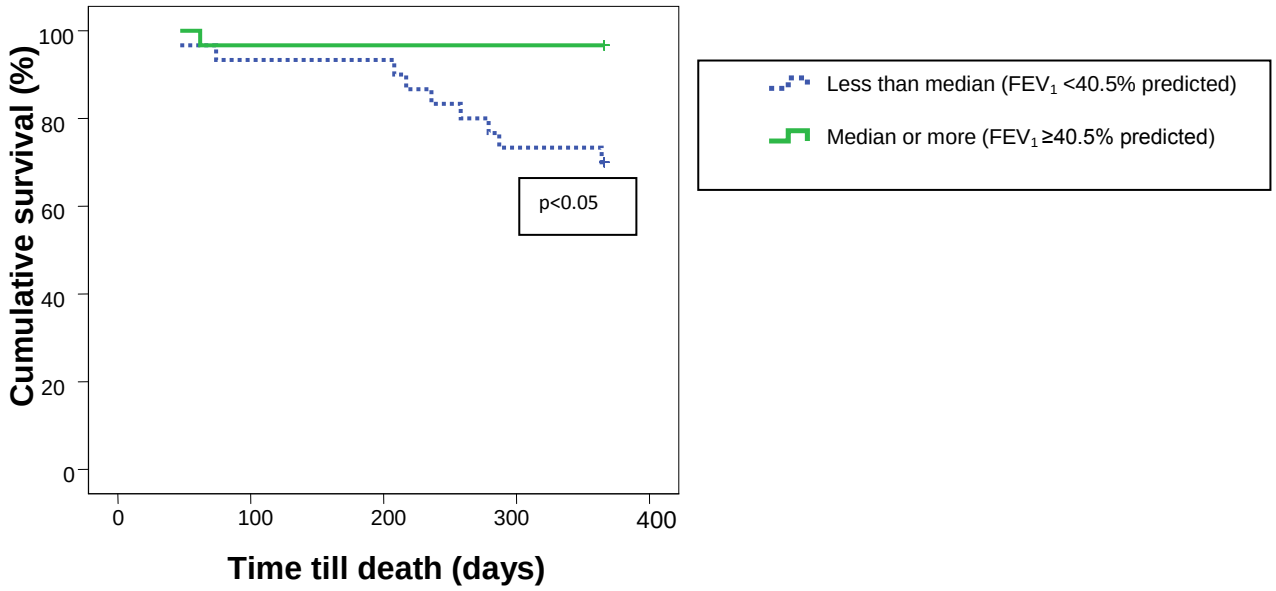


Figure 5.4: Kaplan-Meier plot of 12 month survival according to MRC score

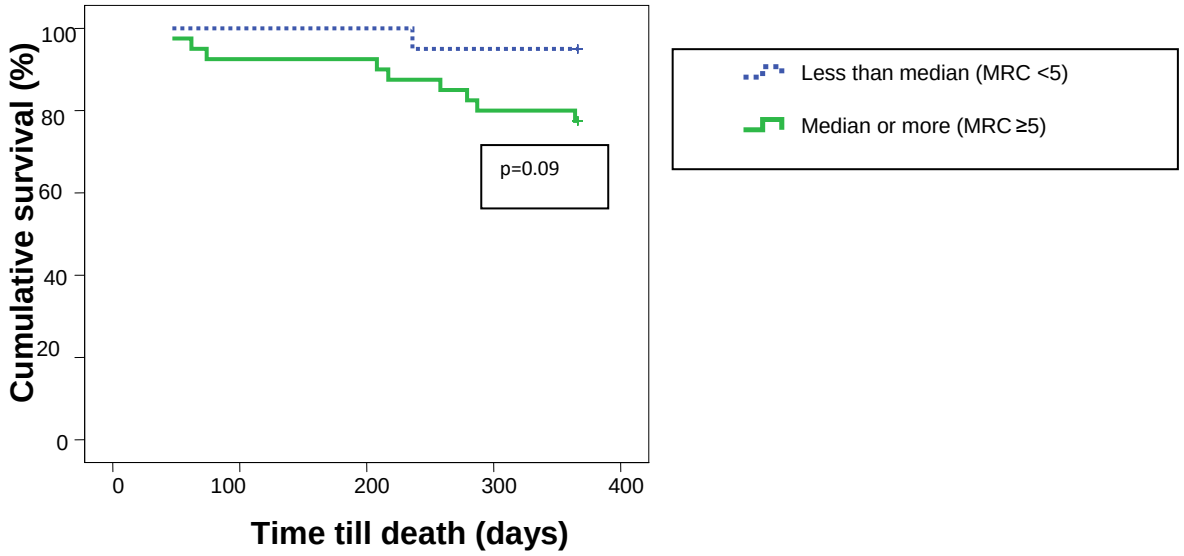


Figure 5.5: Kaplan-Meier plot of 12 month survival according to % time active

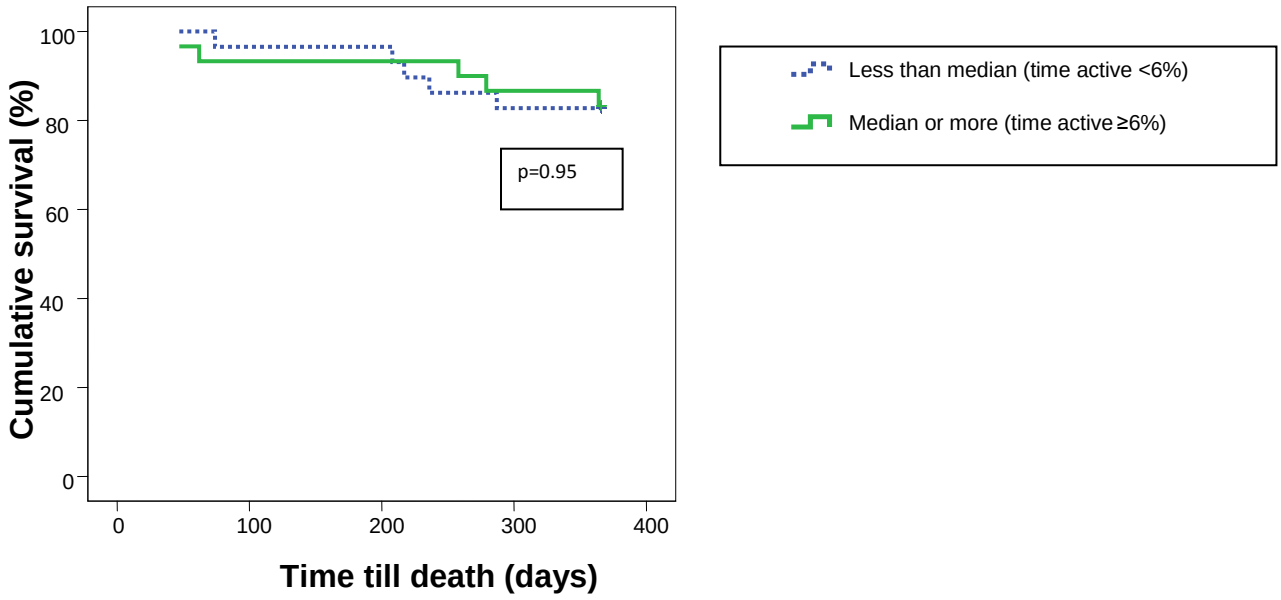
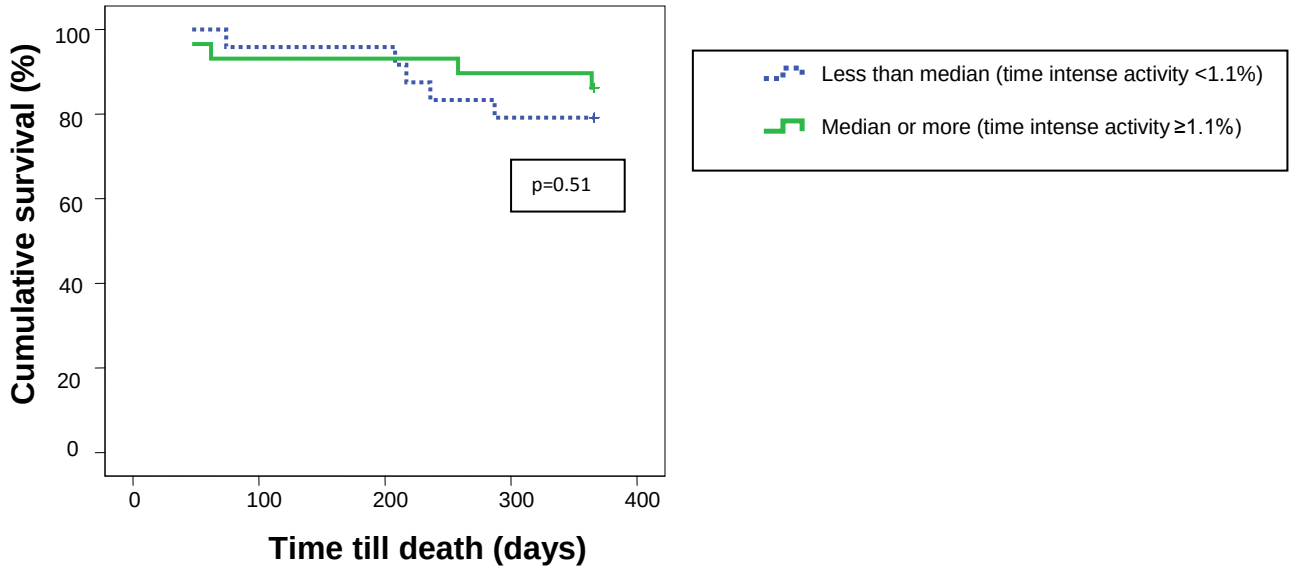


Figure 5.6: Kaplan-Meier plot of 12 month survival according to % time in intense activity



5.3.3 Predictors of readmission at 12 months

Table 5.5 compares the baseline characteristics of patients stratified by 0, 1 or ≥2 readmissions at 12 months. Quadriceps force, MRC, HADa and LCADL predicted readmission. There was a trend towards worse $SGRQ_{TOTAL}$ (and its domains) in patients with ≥2 readmissions, but this did not meet levels of statistical significance. Generally, there were few differences between subjects with 0 readmissions and those with 1 readmission: where there were differences, they tended to distinguish subjects with 2 or more admissions from those with 0 or 1. As with mortality, physical activity recorded by accelerometer at baseline did not predict 12 month readmissions, although there were trends towards lower levels of physical activity as the number of readmissions increased.

Table 5.5: Baseline characteristics (assessment 1) of patients according to readmissions at 12 months (n=50)

Mean (sd)	0 readmissions [n=16]	1 readmission [n=15]	≥2 readmissions [n=19]	p value
Age (yrs)	67.9 (11.0)	69.7 (8.6)	69.7 (8.6)	NS
BMI	31.2 (10.0)	26.6 (8.2)	28.7 (5.7)	NS
FEV_1 (l)	1.0 (0.3)	1.2 (0.6)	1.0 (0.5)	NS
FEV_1 % predicted	43.9 (14.4)	51.3 (21.9)	47.1 (17.8)	NS
FVC (l)	2.0 (0.6)	2.2 (0.8)	1.8 (0.8)	NS
FVC % predicted	68.5 (19.6)	76.9 (17.0)	71.0 (15.5)	NS
QF (kg)*	26.0 [18.8-34.0]	24.2 [18.8-31.8]	17.1 [15.6-23.6]	<0.05** $^{\Psi}$
QF/BMI % ratio	93.8 (36.1)	102.3 (46.4)	71.1 (33.0)	NS
6MW(m)	179 (93)	193 (105)	142 (105)	NS
$SGRQ_{TOTAL}$	68.7 (14.6)	69.3 (20.1)	74.9 (12.1)	NS
MRC*	5 [4-5]	4 [4-5]	5 [5-5]	<0.05$^{\Psi}$
BODE*	6.0 [5.3-8.0]	6.5 [4.8-8.0]	7.0 [7.0-8.0]	NS
HADanxiety	6.9 (4.0)	8.1 (5.1)	12.1 (5.2)	<0.05**
HADdepression	7.2 (4.3)	7.7 (5.0)	8.5 (3.6)	NS
London Chest ADL	39.5 (16.0)	40.1 (15.5)	53.0 (11.0)	<0.05** $^{\Psi}$
Nottingham Extended ADL	12.6 (6.1)	12.9 (4.6)	12.2 (5.1)	NS
% time active*	8.2 [4.0-10.9] [n=15]	7.1 [3.0-10.2] [n=15]	5.7 [3.6-14.6] [n=19]	NS
% time in intense activity*	1.9 [0.2-3.3] [n=14]	1.2 [0.4-2.0] [n=13]	0.9 [0.2-3.5] [n=17]	NS

*Median [interquartile range]

** significant between 0 and ≥2 readmissions

$^{\Psi}$ significant between 1 and ≥2 readmissions

(Bonferroni adjustment for multiple comparisons)

5.3.3.1 Multivariate analysis

Stepwise binary logistic regression analysis was performed, with ≥ 1 readmission at 12 months as the dependent and age, FEV_1, FEV_1 % predicted, FVC, FVC % predicted, quadriceps force, 6MW, BODE, $SGRQ_{TOTAL}$, MRC, HADa, HADd, LCADL, % time active and % time in intense activity as covariates. Only LCADL was a significant predictor of 1 or more readmission at 12 months (Table 5.6.)

Table 5.6: Multivariate analysis output for predictors of of ≥ 1 readmission 12 months after assessment 1: LCADL was the only predictor of ≥ 1 readmission at 12 months

	B	S.E.	Sig.	Exp(B)	95.0% C.I.	
					Lower	Upper
LCADL	.046	.023	0.042	1.047	1.002	1.095
Constant	-1.131	1.005	0.261	0.323		

5.3.3.2 Kaplan Meier plots of admission free survival at 12 months

Figures 5.7-5.13 are Kaplan Meier plots of 12 month admission free survival according to whether the measured parameter was less than or greater than/equal to the median reading. There were significant differences between patients stratified by HADa, and a non significant trend between patients stratified by LCADL score. There was a non-significant trend with respect to FEV_1, quadriceps force and BODE score. In terms of physical activity, there was no statistically significant difference in readmissions, although there was a trend towards increased admission free survival in patients who spent greater time in intense activity at baseline.

Figure 5.7: Kaplan-Meier plot of 12 month admission free survival according to HADa score

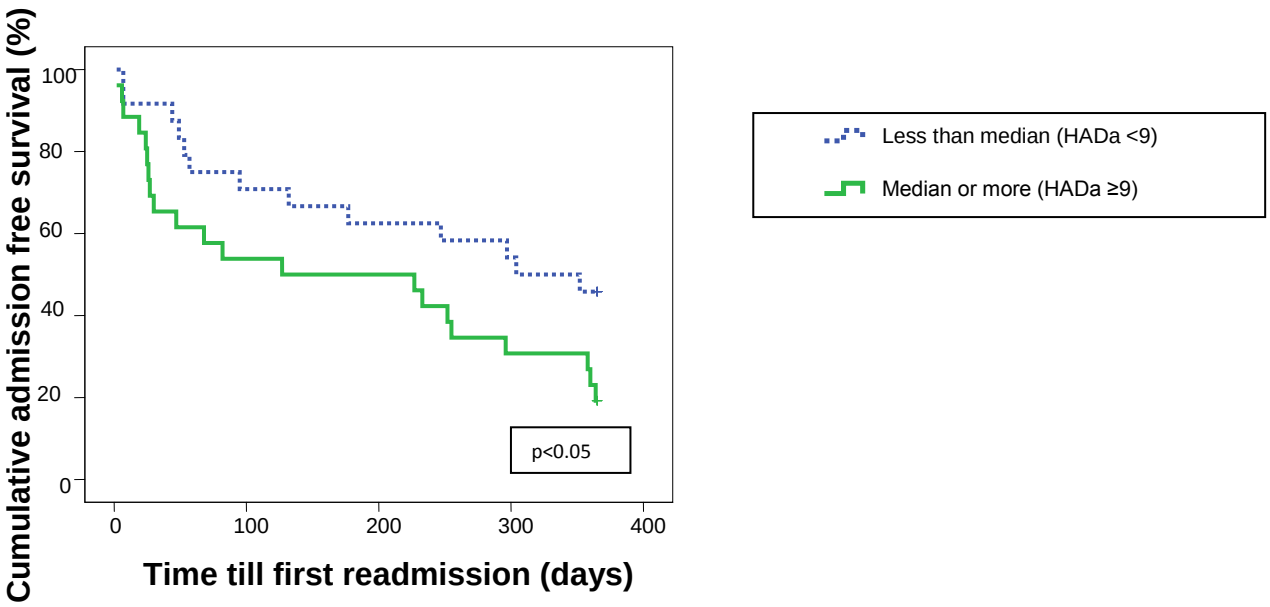


Figure 5.8: Kaplan-Meier plot of 12 month admission free survival according to LCADL score

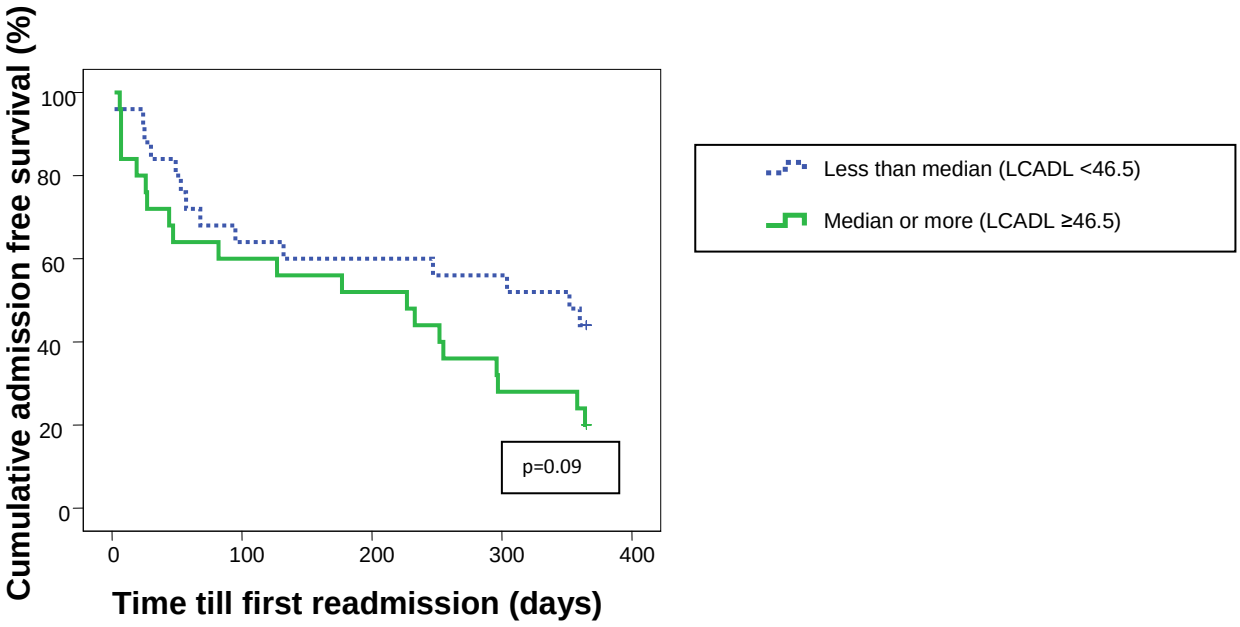


Figure 5.9: Kaplan-Meier plot of 12 month admission free survival according to FEV_1

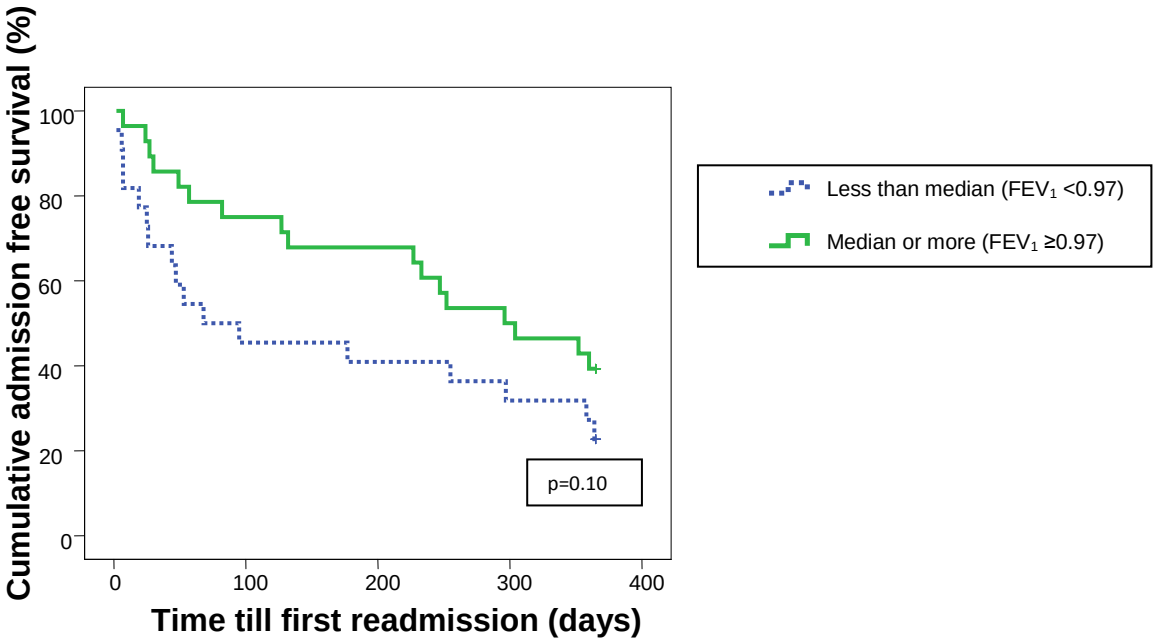


Figure 5.10: Kaplan-Meier plot of 12 month admission free survival according to quadriceps force

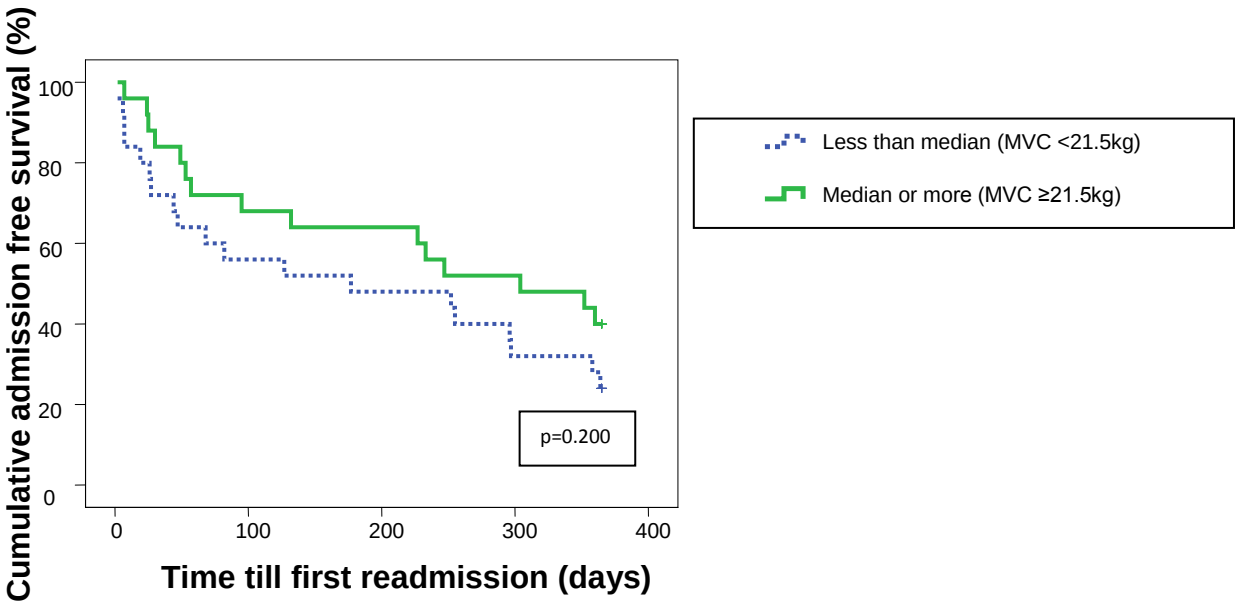


Figure 5.11: Kaplan-Meier plot of 12 month admission free survival according to BODE score

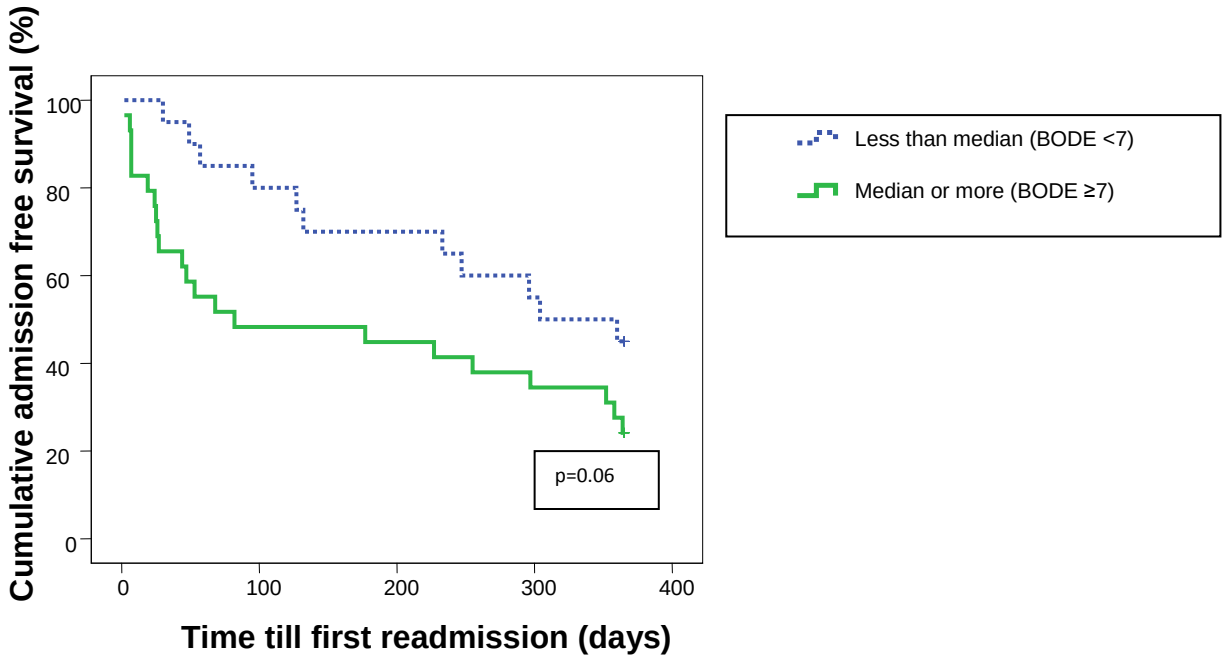


Figure 5.12: Kaplan-Meier plot of 12 month admission free survival according to % time active

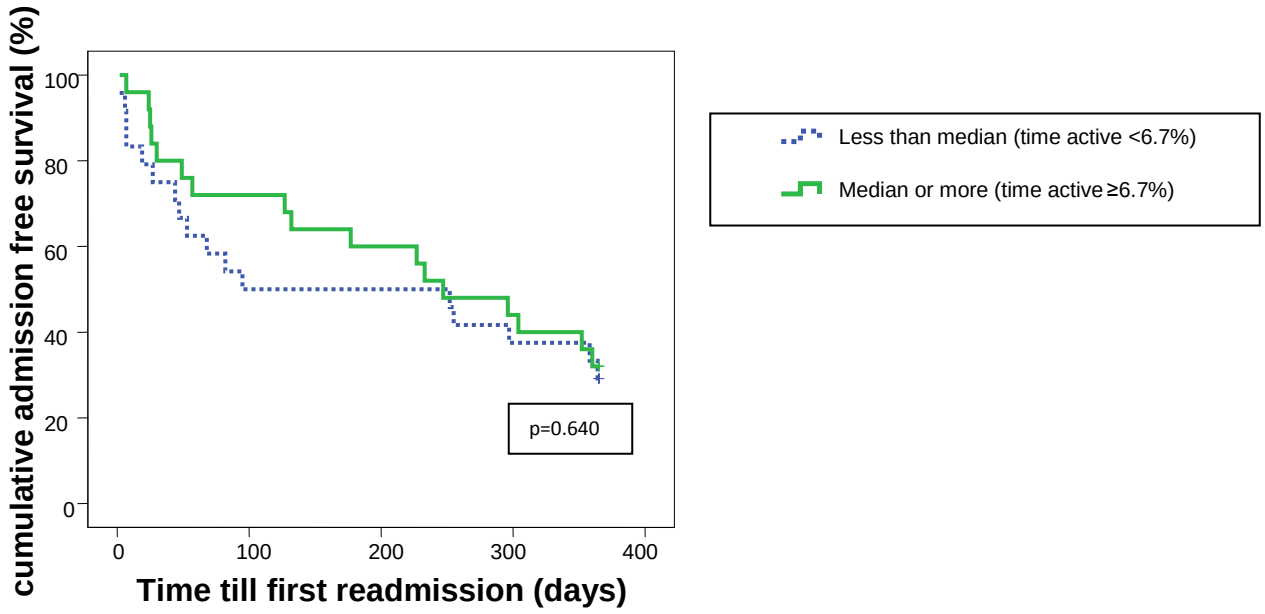
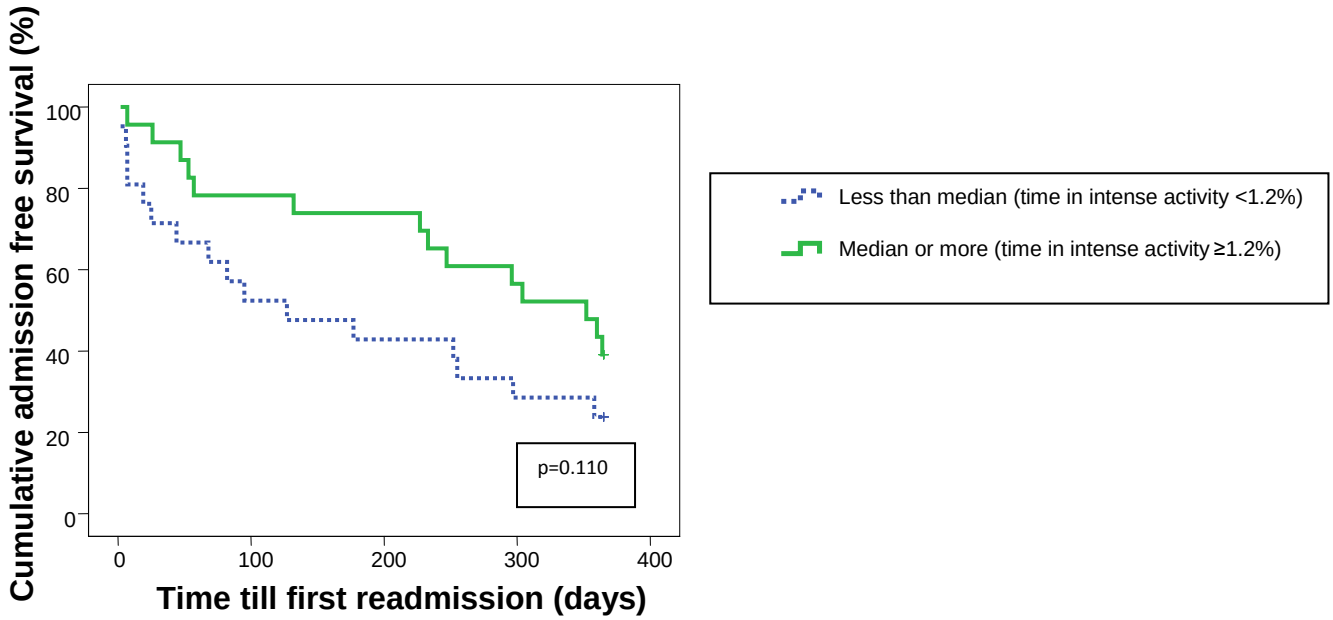


Figure 5.13: Kaplan-Meier plot of 12 month admission free survival according to % time in intense activity



5.3.4 Readmissions and mortality at 12 months and relationship with early home discharge

We have shown in Chapter 4 that early discharge home after the index hospital admission (median length of stay 4 days vs 9 days) was associated with increased physical activity in the early stages of recovery. However, early discharge was not associated with readmission or mortality at 12 months (Tables 5.7 and 5.8).

Table 5.7: Readmission at 12 months and early discharge versus remaining in hospital cross tabulation (Fisher's Exact test)

		≥1 readmission 12 months		
	TOTAL	Yes	No	
Early Discharge	21	13	8	$\chi^2 = 0.73$ NS
Hospital	23	17	6	
TOTAL	44	30	14	

Table 5.8: Mortality at 12 months and early discharge versus remaining in hospital cross tabulation (Fisher's Exact test)

		Dead at 12 months		
	TOTAL	Yes	No	
Early Discharge	25	4	21	$\chi^2 = 0.014$ NS
Hospital	27	4	23	
TOTAL	52	8	44	

5.3.5 Readmissions and mortality at 12 months and relationship with change in health status, quadriceps force, exercise capacity and physical activity

Although there was no overall change in health status, quadriceps force, exercise capacity or physical activity levels between assessments 1 and 3, some patients did improve between assessments. We investigated whether change in these measures between assessments was a predictor of mortality and readmission at 12 months (Table 5.9, 5.10). There was a trend towards SGRQ worsening between assessments 1 and 3 in those who died, whereas it improved in the survivors, although the difference was not statistically significant. Changes in MRC, HADa, HADd, LCADL, NEADL, quadriceps force, 6 minute walk or levels of physical activity were not different between the survivors and those who died. Similarly, changes in these measures were not able to distinguish those who had ≥1 readmission from those who did not. The only measure that reached statistical significance was a paradoxical small fall in % time in intense activity between assessments 1 and 2 in those with no readmissions, versus a small increase in those with ≥1 readmissions. Small numbers have been compared in this part of the analysis, and this is likely to be a type 1 error.

Table 5.9: Changes in measures between assessments in patients who died or were alive at 12 months

Mean (sd) change in	Visit Interval	Alive at 12 mths [n=50]	Dead at 12 mths [n=10]	p value
$SGRQ_{TOTAL}$	V1-V3	-2.3 (7.8) [n=37]	3.2 (8.9) [n=6]	0.12
MRC	V1-V3	0 (0.6) [n=37]	0.2 (0.4) [n=6]	0.45
HADanxiety	V1-V3	0.9 (2.9) [n=37]	0.2 (3.3) [n=6]	0.60
HADdepression	V1-V3	0.6 (2.7) [n=37]	0 (1.8) [n=6]	0.61
London Chest ADL	V1-V3	0.1 (12.2) [n=36]	-4.2 (9.1) [n=5]	0.46
Nottingham Extended ADL	V1-V3	-0.4 (3.2) [n=36]	-2.3 (4.5) [n=6]	0.20
QF (kg)	V1-V2	-0.3 (4.3) [n=22]	0.5 (2.4) [n=5]	0.71
QF (kg)	V1-V3	-0.9 (4.3) [n=32]	-2.6 (5.5) [n=4]	0.47
6MW(m)	V1-V2	28.3 (52.6) [n=22]	8.2 (38.8) [n=4]	0.43
6MW(m)	V1-V3	15.9 (66.4) [n=32]	22.7 (32.3) [n=4]	0.86
% time active	V1-V2	3.2 (5.4) [n=22]	1.4 (7.7) [n=5]	0.55
% time active	V1-V3	1.4 (4.4) [n=37]	-1.2 (5.9) [n=6]	0.20
% time in intense activity	V1-V2	0.8 (2.0) [n=20]	0.7 (1.5) [n=5]	0.94
% time in intense activity	V1-V3	0.4 (1.5) [n=37]	-0.4 (1.1) [n=6]	0.19

Table 5.10: Changes in measures between assessments in patients who had 0 or ≥1 readmissions at 12 months

Mean (sd) change in	Visit Interval	0 readmissions at 12 months [n=16]	≥1 readmission at 12 months [n=34]	p value
$SGRQ_{TOTAL}$	V1-V3	-3.7 (8.2) [n=15]	-1.3 (8.9) [n=22]	0.36
MRC	V1-V3	0 (0.5) [n=15]	0 (0.7) [n=22]	0.83
HADanxiety	V1-V3	1.8 (2.4) [n=15]	0.2 (3.1) [n=22]	0.11
HADdepression	V1-V3	0.9 (3.3) [n=15]	0.4 (2.3) [n=22]	0.63
London Chest ADL	V1-V3	1.3 (15.2) [n=15]	-0.8 (9.9) [n=21]	0.62
Nottingham Extended ADL	V1-V3	0.6 (3.6) [n=15]	-1.0 (2.8) [n=21]	0.13
QF (kg)	V1-V2	-1.0 (6.3) [n=9]	0.2 (2.4) [n=13]	0.51
QF (kg)	V1-V3	-1.1 (4.9) [n=13]	-0.8 (4.0) [n=19]	0.85
6MW(m)	V1-V2	34.4 (57.8) [n=10]	23.2 (49.8)[n=12]	0.63
6MW(m)	V1-V3	37.5 (81.7) [n=13]	1.1 (50.8) [n=19]	0.13
% time active	V1-V2	1.1 (4.2) [n=10]	5.0 (5.7) [n=12]	0.09
% time active	V1-V3	1.5 (4.6) [n=15]	1.4 (4.4) [n=22]	0.96
% time in intense activity	V1-V2	-0.4 (1.4) [n=8]	1.5 (2.0) [n=12]	0.03*
% time in intense activity	V1-V3	0.1 (1.5) [n=14]	0.6 (1.5) [n=23]	0.32

5.3.6 Relationships between admissions in the previous 12 months and patient characteristics at initial assessment

10 patients had been admitted to hospital once with a COPD related condition in the previous 12 months, 27 patients had been admitted twice or more, and 23 had not been admitted in that time period. Table 5.11 demonstrates the characterisics at baseline of subjects according to hospitalisation in the previous 12 months. Because of the relatively low number of patients who had been admitted once, patients were classified simply by 0 admissions or ≥1 readmission. Patients who had not been admitted in the previous 12 months had significantly greater FEV_1, FVC and quadriceps force, and significantly lower hospital anxiety, depression and LCADL scores than patients who had been hospitalized. There was a trend towards lower $SGRQ_{TOTAL}$ and BODE, and greater 6MW and % time active and in intense activity in the patients without prior admission, but these did not reach levels of statistical significance.

Table 5.11: Baseline characteristics (assessment 1) of patients with 0 or ≥1 admissions in the previous 12 months (n=60)

Mean (sd)	0 admissions in previous 12 months [n=23]	≥1 admission in previous 12 months [n=37]	p value
Age (yrs)	67.3 (10.1)	70.2 (8.0)	NS
BMI	29.7 (9.5)	27.4 (6.3)	NS
FEV_1 (l)	1.1 (0.5)	0.9 (0.4)	<0.05
FEV_1 % predicted	48.4 (19.7)	42.5 (16.3)	NS
FVC (l)	2.2 (0.7)	1.8 (0.6)	<0.05
FVC % predicted	71.1 (17.4)	68.4 (17.2)	NS
QF (kg)*	26.9 [18.6-35.7]	19.4 [16.7-24.6]	<0.05
QF/BMI % ratio	101.4 (45.0)	83.6 (36.2)	NS
6MW(m)	195 (120)	152 (86)	NS
$SGRQ_{TOTAL}$	68.0 (18.2)	74.3 (11.9)	NS
MRC*	5 [4-5]	5 [4-5]	NS
BODE*	6.5 [5.0-8.0]	7.0 [6.0-8.0]	NS
HADanxiety	7.0 (4.6)	10.3 (4.8)	<0.05
HADdepression	6.7 (4.3)	9.0 (3.8)	<0.05
London Chest ADL	39.5 (15.6)	48.7 (13.3)	<0.05
Nottingham Extended ADL	12.9 (6.3)	11.8 (4.7)	NS
% time active*	7.4 [4.0-10.6] [n=23]	5.4 [3.3-10.7] [n=36]	NS
% time in intense activity*	1.5 [0.2-2.9] [n=22]	0.9 [0.2-2.6] [n=31]	NS

*Median [interquartile range]

5.4 Discussion

10/60 (17%) of patients died and 34/50 (68%) had one or more COPD related readmission within 12 months of the initial assessment. We have shown that baseline spirometry and overall BODE score predicted mortality in this patient group, while baseline peripheral muscle strength and self reported breathlessness, anxiety and perception of ability to perform ADL's predicted readmission at 12 months. Actual levels of physical activity recorded by accelerometer at baseline did not predict mortality or readmission, although there was a trend towards greater admission free survival in patients who spent more time in intense activity. Changes in either of these measures of physical activity between assessments did not predict readmission or death. Patients who had received an early discharge home were not more likely to avoid readmission or death than those who had remained in hospital for longer. Baseline spirometry, peripheral muscle strength and self reported anxiety, depression and respiratory specific ADL limitation were related to hospitalisation status in the previous 12 months.

Previous studies have reported that prior exacerbations predicted subsequent exacerbations(34, 198) and that previous admissions predicted subsequent admissions(43), however, we did not identify a significant relationship. Hurst's analysis of exacerbations among 2138 patients enrolled in the ECLIPSE study found that a history of exacerbations was the most important determinant of frequent exacerbations(199). However, ECLIPSE patients were not recruited on the basis of exacerbation history and only 47% of patients in that study had exacerbated in the 12 months prior to the commencement of the study; additionally, many of these exacerbations did not require hospital admission. In contrast, 62% of patients in our group had been hospitalised in the 12 months prior to the first assessment, and 68% were readmitted at least once in the following 12 months. It may be that we have

studied a patient group that is already an exacerbator phenotype, who have already suffered frequent exacerbations and admissions and continue to do so. The admission that constituted their first assessment for this study may not have been a sentinel event for many of our patients; we may have simply picked them up at some point in their journey through recurrent exacerbations.

The 12 month mortality rate of 17% and readmission rate of 62% compares to 6% and 35% reported by Osman et al(42), 23% and 55% reported by Groenewegen et al(35) and 29% and 63% reported by Garcia-Aymerich et al(43). Patients in these previous three studies were of comparable age (68-71 years) but tended to have worse spirometry (FEV_1 36-39% predicted) than our group. Groenewegen included patients who died during the admission, as did Garcia-Aymerich, whose follow up time was more than 1 year (mean 410 days) and who excluded only patients who died without readmission from the readmission data. Considering that our patients had better spirometry, did not have respiratory acidosis or significant other co morbidity and all patients survived to discharge, this may explain the slightly lower mortality rates than those reported by Groenewegen and Garcia-Aymerich. However, our comparable readmission rates suggest that our patient group is more frail than those studied previously, and this may be reflected in the $SGRQ_{TOTAL}$ of 71.9 in our patient group, in comparison to 52.7 in Osman's group.

In Chapter 4, we demonstrated that physical activity and health related quality of life, although not related to each other, predicted readmission and re exacerbation at 4 months. However, this was not the case with respect to readmission at 12 months, or for admission in the previous 12 months. We have presented the baseline physical activity since the highest number of subjects was assessed at this visit. However, there was also a lack of relationship between physical activity 1 month after discharge and previous or subsequent admission, in contrast to Pitta's findings in a small number of patients(77). However, self reported physical

activity as measured by LCADL did predict readmission in our patients, as it did in Garcia-Aymerich's 340 patients (using a Spanish adaptation of the Minnesota Leisure Time Physical Activity Questionnaire)(43). Exercise capacity did not predict readmission in our patient group: 6 minute walk distance was not a reliable predictor of readmission in Pitta's group either(77), although it has been shown to predict hospitalisation in a group of stable COPD subjects(200). We have previously shown that, in relation to physical activity, what COPD patients say they can do correlates with what they can do, but these measures do not correlate well with what they actually do. However, it may be the case that the patient's perception of their breathlessness and ability to carry out physical activities are the most important features that determine future events, particularly readmissions. Osman has previously shown that health status as measured by SGRQ and its domains predicted readmission(42). Although similar trends were present in our patient group, these were not statistically significant.

A limitation of these data is that we measured readmissions to University Hospital Aintree. Although patients would usually be readmitted to the same hospital since this is determined by their home address, it is possible that some patients, who were on vacation or staying with relatives for example, would have been readmitted to another hospital and we will not have captured these episodes in our data analysis. However, we do not expect that there were many such episodes. A further limitation of these data is the relatively small number of patients in comparison to some previous studies and this may be particularly relevant with respect to the mortality data. This may be a reason why quadriceps strength failed to predict mortality in this patient group in contrast to Swallow's findings in stable COPD patients(76), although it did predict readmission. While it is recognised that the BODE score is a useful prognostic indicator in COPD(53), in this group of exacerbators, the ability of BODE to predict mortality at 12 months on univariate analysis is driven by the baseline FEV1 component: there appears to be no prognostic benefit in additionally measuring MRC, BMI or 6MW in

patients in the early stages of recovery from exacerbation. Previous work on predictors of mortality following admission for exacerbation have yielded mixed data. Connors identified age, self reported activity score and BMI as independent predictors of survival time(40), while Groenewegen identified long term oral corticosteroid use, increased $PaCO_2$ and older age as risk factors(35). The only consistent predictor between the two studies was age, but we did not identify this as a factor.

It is recognised that COPD patients suffer from high levels of anxiety symptoms and these may be related to health outcomes(59, 201). In our patient group, anxiety was a predictor of admission in the previous 12 months and readmission in the following 12 months. This is consistent with Eisner's study of 1202 COPD patients, where anxiety (also measured with the HAD questionnaire) was related to a higher risk of COPD exacerbation(202). The reason why the ability of physical activity to predict readmission at 4 months was lost at 12 months may be a floor effect. While 45% of patients had been readmitted at 4 months, 68% had been readmitted at 12 months: it may be the case that the group as a whole had become more homogenous with time, caught in the recognised cycle of exacerbation, worsening health status and functional decline. This, coupled with the poor health related quality of life in the whole patient group at the outset, may be a reason why it became more difficult to differentiate the patients with time. This may also explain why the relationship between spirometry and previous admission is lost in predicting readmission, although it is interesting to note that peripheral muscle strength remained a predictor of both readmission at 12 months and admission in the previous 12 months.

It therefore appears that the factors related to readmission and mortality differ, perhaps because readmission is likely to be determined by psychological and social factors, therefore explaining why self reported perception of breathlessness, anxiety and physical activity limitation were determinants of readmission.

As previously discussed, this appears to be a particularly frail group of COPD patients who show little recovery from the initial hospitalisation, and it may be the exacerbations themselves and associated systemic inflammation that are driving decline in these patients irrespective of lung physiology, health status or levels of physical activity. When patients are discharged home from hospital following an exacerbation, the majority do not feel informed about their condition, ready to leave hospital or able to cope at home(203). This may be a partial explanation for why many patients do not recover from their initial hospitalisation and why readmission rates are so high. Delivering early pulmonary rehabilitation after exacerbation may help to resolve some of these issues. While there is evidence that early PR post exacerbation improves health status and peripheral muscle strength and also reduces hospital admissions and mortality in the short term(196, 197, 204), it is not clear whether there are certain COPD patients who do not gain these benefits, and who they are. Moreover, as with PR for stable COPD, there is a lack of data that the benefits from post exacerbation PR persist in the longer term. These are areas that require further investigation.

Chapter 6: Physical activity after pulmonary rehabilitation

6.1 Introduction

Pulmonary rehabilitation (PR) is a multi-disciplinary intervention which encompasses a programme of high intensity exercise training, disease education and psychosocial support with the aim of reversing deconditioning, optimising functional capacity and both controlling and alleviating symptoms.

In the past decade, PR has been established as a very important non pharmacological treatment for COPD. PR improves exercise tolerance, functional capacity, health related quality of life and reduces the number of hospitalizations(64, 125). It also improves dyspnoea and fatigue and enhances patients' sense of control over their condition(205). In recent years, there has been interest in assessing whether the improvements gained through PR translate to increased participation in activities of daily living. Several studies have assessed this with pedometers or accelerometers: some demonstrated statistically significant improvement in physical activity after PR(166, 169, 170), while others did not(171, 206, 207). Activity monitors have also been used to give feedback to the patient during the course of PR(208). Although the benefits of pulmonary rehabilitation compared with control subjects are seen at the end of the treatment course and for a few months afterwards, there appears to be a decline towards baseline in exercise capacity and health status after 9-18 months(126-128). It is not clear whether levels of physical activity follow the same pattern and whether any improvements immediately after the course of PR are subsequently lost.

In this prospective cohort study, our primary aim was to investigate levels of physical activity in a group of COPD subjects using the DynaPort before and after a course of PR and 6 months later. Secondary aims were to investigate breathlessness scores, health related quality

of life, self reported physical activity and exercise capacity, and to investigate the relationships with each other.

6.2 Methods

Recruitment for this study was January 2007 to May 2008. Patients were referred by a hospital based practitioner (either a doctor or respiratory nurse specialist) at University Hospital Aintree to the respiratory physiotherapist to be considered for PR. At the time of initial assessment, the physiotherapist verified documentation in the medical notes of a diagnosis of COPD and determined the patient's suitability for PR; patients were then invited to participate in the study by the physiotherapist. Exclusions were a COPD exacerbation (requiring oral corticosteroids, antibiotics or both) in the 4 weeks prior to commencing PR, unstable cardiac or rheumatological disease, large abdominal aortic aneurysm, significant disease other than COPD which would significantly affect mobility or daily activity, significant cognitive impairment or participation in a course of PR in the previous 2 years. Patients with unstable cardiac or rheumatological disease, significant disease other than COPD, which would significantly affect mobility or daily activity, or significant cognitive impairment were not offered rehabilitation. If subjects had suspected COPD without available confirmatory spirometry, they were enrolled into the study, but were subsequently excluded if post bronchodilator FEV_1 was greater than 80% predicted or if the FEV_1/FVC ratio was 70% or greater. Participating subjects gave oral and written consent. The study was approved by South Sefton Ethics Committee.

Assessment 1

This was carried out after the initial physiotherapist assessment, before PR began. A proforma was completed detailing co morbidities, medication, smoking status and social history, vaccinations and exacerbation status. Measures of height, weight and bioimpedance were made. From the impedance, estimates of fat free mass (FFM) were calculated using a disease-specific equation(180) Measurements of post bronchodilator spirometry (FEV_1, FVC), slow vital capacity, inspiratory capacity (IC), total lung capacity (TLC), residual volume (RV) and gas transfer (TLCO and KCO) were recorded. Quadriceps force (QF) and Endurance Shuttle Walk (ESWT) were assessed. Subjects completed St George's Respiratory Questionnaire (SGRQ), MRC dyspnoea scale, hospital anxiety and depression score (HAD), Chronic Respiratory Questionnaire -self reported (CRQ-SR), London Chest Activities of Daily Living Score (LCADL) and Nottingham Extended Activities of Daily Living Questionnaire (LCADL). Subjects were then asked to wear the DynaPort (DP) for 2 full consecutive days at home.

Pulmonary Rehabilitation

The patient started PR within 7 days of the visit 1 assessment. This was an 8 week course of treatment, carried out twice per week in the afternoon (either Monday/Thursday or Tuesday/Friday). Most patients received the PR in the physiotherapy department at University Hospital Aintree, while some received it at a community centre in Litherland, Liverpool, depending on which venue was more convenient for the patient. There was a maximum of 10 patients in each PR group. The first hour would consist of exercises (including 5 minutes warm up and 5 minutes cool down at the end), supervised by a respiratory physiotherapist and an assistant. The exercises performed were upper and lower limb exercises which comprised: treadmill, recliner bike, static bike, stepper machine,

trampette, step, wall press-ups, sit-to-stand, bicep curls with weights, shoulder raises with weights, deltoid raises with weights and toe raises. Patients were encouraged to move to a new exercise every 5 minutes. Although there were no fixed rest periods, patients either took them as they required, or were advised to take them on the judgement of the physiotherapist. Patients did not do every exercise: this was based on the abilities and choice of the patient and physiotherapist judgement. The physiotherapist documented exactly what level and how much of each exercise the patient did at each session. The patient would be encouraged to increase the speed, level or intensity with which they performed each exercise as they progressed through the 8 week course, guided mainly by the degree of breathlessness on carrying out each activity; the change was documented.

If the patient used ambulatory oxygen, or if they significantly desaturated during the exercise (a fall in oxygen saturations of at least 4% below 90%) then they were provided with oxygen while carrying out these exercises.

In the hour following the exercise session, there would be a variety of educational sessions over the 8 week course, encompassing information about COPD and advice on inhaler devices, smoking cessation, vaccinations and dietary modification. Education and psychosocial input about breathing control exercises to help cope with breathlessness and anxiety were also provided. If patients exacerbated during the PR course and missed sessions, then the PR course was prolonged so that patients received a total of 16 sessions.

Assessment 2

A subgroup of patients carried out this assessment half way through the course, after 8 sessions (4 weeks) of PR. Subjects were asked to wear the DynaPort for 2 full consecutive days at home. No other measures were made. The DynaPort was not worn on days when PR

took place. Only some patients were asked to do this assessment, according to availability of the DynaPort equipment and being able to fit the equipment on non PR days at this specific time.

Assessment 3

This was carried out within 7 days of the patient finishing the course of PR. Any exacerbations (requiring oral corticosteroids, antibiotics or both), hospitalisations or changes in treatment since the first visit were recorded. All the measures taken at assessment 1 were repeated at this visit. Subjects were then asked to wear the DynaPort for 2 full consecutive days at home.

Assessment 4

This was carried out 6 months after finishing the course of PR. Exacerbations, hospitalisations and changes in treatment since the previous visit were recorded, as well as an update on co morbidities, smoking status and vaccination history. All the measures taken at assessments 1 and 3 were repeated at this visit. Subjects were then asked to wear the DynaPort for 2 full consecutive days at home.

Statistical Analysis

Statistical analysis was carried out using SPSS (15.0). Variables were tested for skewdness and Normality using the Shapiro-Wilks test. Mean (sd) values were calculated and non-Normally distributed variables were expressed as median [interquartile rang]). Paired parametric variables were analysed by a paired t test. Non parametric variables were analysed by a Mann-Whitney U test or Wilcoxon signed-rank test where the data were coming from

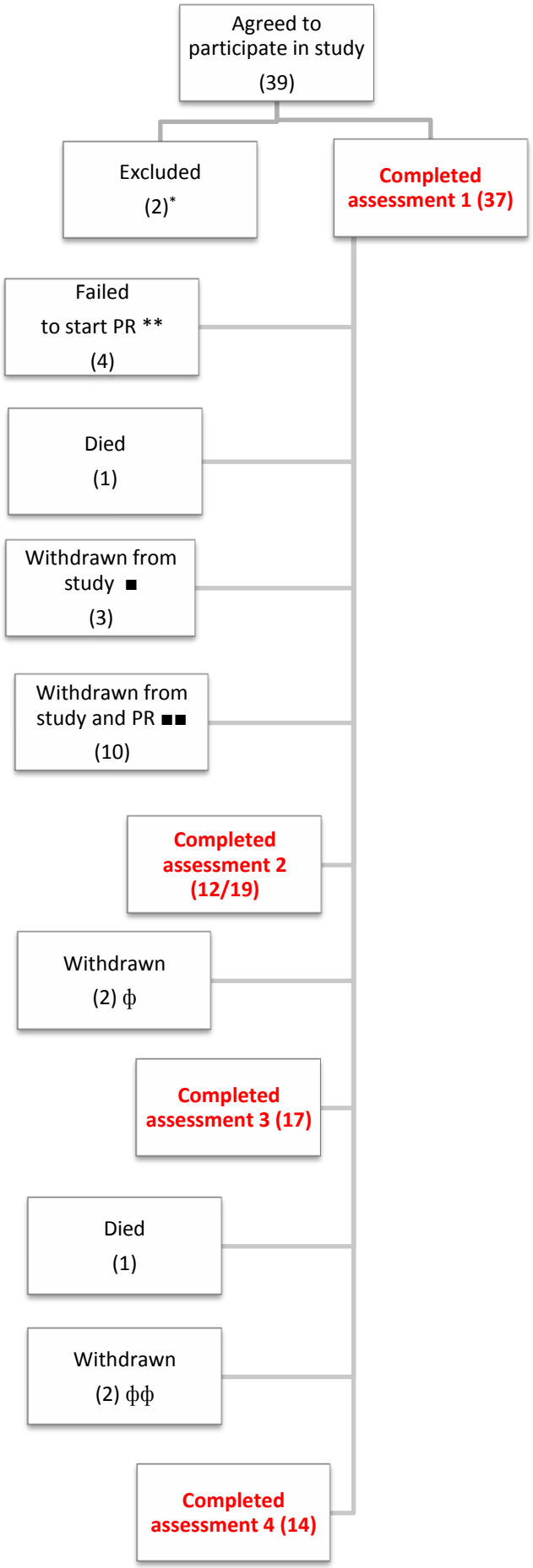
the same subjects. Where 3 or more measures were analysed from the same participants, comparisons were made using one way repeated measures analysis of variance (ANOVA) or Friedman's ANOVA (non parametric variables). When the p value was <0.05 then a post hoc test was performed. A Pearson correlation test was performed to assess relationships. A level of significance was set at 0.05 for all statistical tests except for where multiple comparisons were made, when $p<0.01$ was accepted as significant. No attempt was made to assume missing data from subjects who were lost to follow up.

6.3 Results

6.3.1 Flow and follow up of subjects

Figure 6.1 shows the progress of subjects through the study. 39 patients, after initial assessment by the physiotherapist, agreed to participate in the study. 2 patients were subsequently excluded as they did not have COPD based on spirometry and 37 patients completed the first assessment. 4 patients failed to start PR. 1 patient died, 10 patients withdrew from both the study and PR, and 3 patients withdrew from the study before they had completed half of the PR sessions (the reasons are stated in figure 7.1). Of the 19 patients remaining in the study after 4 weeks of PR, 12 patients wore the DynaPort (assessment 2). A further 2 patients withdrew in the second half of the PR course, leaving 17 patients who completed assessment 3 (end of PR). Over the next 6 months, 1 patient died and 2 further patients withdrew from the study, so that 14 patients completed the final visit (assessment 4). 7 of the 37 patients who completed the first assessment were participants in the Litherland community programme. Of these, 2 patients failed to start PR and 3 withdrew during the PR course, leaving only 2 Litherland subjects who completed assessment 3.

Figure 6.1: Flow of participants through the study



*$FEV_1 \geq 80\%$ predicted(2)

** Could not be contacted/ not interested in starting(4)

■ Too tired(1), found the study too time-consuming(2)

■ ■ Too frail to continue(2), personal circumstances(2), further exacerbations- unable to resume PR(4), lost interest(2)

Φ further exacerbations- unable to resume PR(1), lost interest(1)

ϕ ϕ Too frail to attend(2)

Pharmacotherapy

Of the 37 patients who completed assessment 1, 29 were on triple therapy (long acting beta agonist [LABA] + corticosteroid [ICS] + long acting antimuscarinic [LAMA]), 5 were on LABA + ICS, 1 on LAMA + ICS and 2 patients were receiving ICS only. All subjects also used a prn short acting beta agonist.

Assessment for Normality and Skewdness

All data were Normally distributed with the exception of FVC, QF, $SGRQ_{SYMPTOMS}$, $SGRQ_{ACTIVITY}$, MRC, ESWT, % time weightbearing, active and walking. After logarithmic transformation, these variables were Normally distributed with the exception of $SGRQ_{SYMPTOMS}$, $SGRQ_{ACTIVITY}$ and MRC.

6.3.2 Baseline Assessment of Patients (Assessment 1)

The mean (sd) age of the patients was 67.7 (9.6) years. 19 patients were female, 18 male. The mean FEV_1 was 1.1 (0.4) l, 46.9 (16.0) % predicted. 17 subjects were GOLD stage II, 13 were GOLD stage III, and 7 were GOLD stage IV. The median quadriceps force was 25.8 [IQR 20.5-29.7] kg, 65.6 (18.3) % predicted with median ESWT distance of 119 [IQR 30-155] metres. Mean $SGRQ_{TOTAL}$ was 65.6 (14.4). Subjects spent a median 24.0 [IQR 16.9-36.0] % of the time in weightbearing activities (standing and walking), 9.8 [IQR 5.6-15.0] % of the time active and 3.7 [IQR 1.9-5.8] % of the time walking.

Table 6.1: Characteristics of patients before starting pulmonary rehabilitation

Mean (sd)	n=37
Age (yrs)	67.7 (9.6)
FEV_1 (l)	1.1 (0.4)
FEV_1 % predicted	46.9 (16.0)
FVC (l)*	2.3 [1.8-2.3]
FVC % predicted	80.1 (16.4)
RV/TLC ratio (%)	56.1 (9.5)
TLCO	3.6 (1.5)
TLCO % predicted	47.3 (18.0)
BMI	26.3 (5.9)
FFM (kg)	46.3 (8.3)
QF (kg)*	25.8 [20.5-29.7]
QF % predicted	65.6 (18.3)
ESWT distance (m)*	119 [30-155]
$SGRQ_{SYMPTOMS}$*	76.8 [61.6-85.2]
$SGRQ_{ACTIVITY}$*	85.9 [76.0-92.5]
$SGRQ_{IMPACT}$	53.2 (18.1)
$SGRQ_{TOTAL}$	65.6 (14.4)
MRC*	4 [4-5]
$CRQ_{DYSPNOEA}$	2.2 (0.9)
$CRQ_{FATIGUE}$	3.2 (1.3)
$CRQ_{EMOTIONS}$	4.0 (1.4)
$CRQ_{MASTERY}$	4.0 (1.5)
London Chest ADL	34.5 (11.6)
Nottingham Extended ADL	13.4 (4.9)
HADa	8.5 (4.8)
HADd	8.2 (3.2)
% time weight bearing*	24.0 [16.9-36.0] [n=33]
% time active*	9.8 [5.6-15.0] [n=35]
% time walking*	3.7 [1.9-5.8] [n=33]

*Median [interquartile range] (not Normally distributed)

6.3.3 Predictors of failure to complete pulmonary rehabilitation

Of the 37 patients who completed the initial visit (assessment 1), 1 patient died and 3 patients withdrew from the study but not PR. Of the remaining 33 patients, 17 patients completed the course of PR and 16 did not (Figure 6.1). Table 7.2 compares the baseline characteristics of patients who completed PR and those who did not. The only statistically significant predictor of failure to complete PR in this small number of patients was an increased RV/TLC ratio. There was a trend towards lower baseline FEV_1 ,FVC and TLCO, fat free mass and

quadriceps force in those who did not complete PR, although self reported breathlessness, health related quality of life, anxiety and depression and physical activity were comparable in the 2 groups. Neither ESWT distance nor actual physical activity was significantly different between the 2 groups, although there was a trend towards lower baseline ESWT distance in subjects who managed to complete PR.

Table 6.2: Characteristics of patients who completed pulmonary rehabilitation and those who did not

Mean (sd)	Completed PR (n=17)	Did not complete PR (n=16)	p value
Age (yrs)	67.9 (8.0)	65.3 (10.8)	NS
FEV_1 (l)	1.2 (0.4)	1.0 (0.3)	NS
FEV_1 % predicted	48.3 (16.1)	44.7 (15.4)	NS
FVC (l)*	2.6 [1.9-3.4]	1.9 [1.7-2.7]	NS
FVC % predicted	82.8 (14.0)	77.0 (17.5)	NS
RV/TLC ratio (%)	53.2 (8.9)	59.9 (9.3)	<0.05
TLCO	4.0 (1.6)	3.4 (1.5)	NS
TLCO % predicted	52.0 (17.6)	45.1 (18.3)	NS
BMI	27.4 (4.5)	26.0 (7.5)	NS
FFM (kg)	49.3 (7.9)	44.1 (8.8)	NS
QF (kg)*	27.1 [21.6-29.3]	23.8 [19.3-30.2]	NS
QF % predicted	64.6 (20.1)	64.7 (18.0)	NS
ESWT distance (m)*	102 [20-139]	120 [40-160]	NS
$SGRQ_{SYMPTOMS}$*	78.3 [58.2-86.1]	77.9 [65.4-85.8]	NS
$SGRQ_{ACTIVITY}$*	85.8 [79.0-89.5]	92.3 [67.9-92.5]	NS
$SGRQ_{IMPACT}$	52.8 (18.6)	52.7 (18.0)	NS
$SGRQ_{TOTAL}$	65.2 (14.4)	65.5 (14.7)	NS
MRC*	4 [4-5]	4 [4-4.75]	NS
$CRQ_{DYSPNOEA}$	2.4 (1.1)	2.2 (0.6)	NS
$CRQ_{FATIGUE}$	3.3 (1.5)	3.1 (1.0)	NS
$CRQ_{EMOTIONS}$	4.1 (1.6)	3.9 (1.3)	NS
$CRQ_{MASTERY}$	4.3 (1.6)	3.8 (1.3)	NS
London Chest ADL	33.8 (12.9)	36.1 (11.3)	NS
Nottingham Extended ADL	13.3 (4.5)	12.6 (5.0)	NS
HADa	8.9 (5.5)	8.2 (4.7)	NS
HADd	8.7 (3.6)	8.1 (2.8)	NS
% time weight bearing*	25.0 [19.2-36.7] [n=16]	27.1 [15.7-38.9] [n=14]	NS
% time active*	9.8 [6.5-12.0] [n=17]	9.5 [5.6-18.9] [n=15]	NS
% time walking*	3.8 [2.0-5.4] [n=16]	3.5 [2.2-7.8] [n=14]	NS

*Median [interquartile range]

6.3.4 Changes before and after pulmonary rehabilitation

Table 6.3 compares the characteristics before and just after PR of the 17 patients who completed the course. A number of readings of the DynaPort were invalid or incomplete (incorrect set up, premature device switch off and displacement of a lead or the waist belt) as discussed in Chapter 2. When this occurred, patients were requested to repeat the readings. However, some subjects were unwilling to wear the DP again or commenced PR before they had the opportunity to wear the device as part of assessment one. In 2 patients the reading failed for the second time. Therefore, paired readings (before and after PR) were available for only 9 subjects for % time weight bearing, 16 patients for % time active and 11 patients for % time walking (when the waist belt had displaced measurements of % time moving and walking were possible, and when the limb lead had displaced measurements of % time moving were possible). Significant improvements in QF, ESWT, HADd, % time active and % time walking were demonstrated at the end of PR. A statistically significant decline in FVC was also seen, which is difficult to explain, particularly in the context of no changes in any other measure of lung physiology.

Table 6.3: Characteristics of patients before and after pulmonary rehabilitation (n=17)

Mean (sd)	Assessment 1 (pre PR)	Assessment 3 (post PR)	p value
FEV_1 (l)	1.1 (0.4)	1.1 (0.3)	NS
FEV_1 % predicted	47.8 (16.5)	46.9 (18.9)	NS
FVC (l)*	2.6 [1.9-3.4]	2.4 [1.8-3.0]	<0.05
FVC % predicted	82.1 (14.2)	75.5 (18.4)	<0.05
IC (l)	1.8 (1.1)	1.8 (1.1)	NS
RV/TLC ratio (%)	54.1 (8.3)	55.1 (11.6)	NS
TLCO	4.1 (1.5)	4.1 (1.6)	NS
TLCO % predicted	54.6 (15.7)	52.5 (19.6)	NS
FFM (kg)	49.3 (7.9)	48.9 (7.6)	NS
QF (kg)*	27.1 [21.6-29.3]	28.8 [23.6-35.8]	<0.05
ESWT distance (m)*	102 [20-139]	172 [60-380]	<0.05
$SGRQ_{SYMPTOMS}$*	78.3 [58.2-86.1]	80.9 [56.7-94.0]	NS
$SGRQ_{ACTIVITY}$*	85.8 [79.0-89.5]	85.8 [74.5-92.3]	NS
$SGRQ_{IMPACT}$	52.8 (18.6)	51.6 (21.9)	NS
$SGRQ_{TOTAL}$	65.2 (14.4)	64.5 (17.8)	NS
MRC*	4 [4-5]	4 [4-5]	NS
$CRQ_{DYSPNOEA}$	2.3 (1.1)	2.3 (1.0)	NS
$CRQ_{FATIGUE}$	3.3 (1.5)	3.5 (1.4)	NS
$CRQ_{EMOTIONS}$	4.1 (1.6)	4.4 (1.4)	NS
$CRQ_{MASTERY}$	4.3 (1.6)	4.9 (1.5)	NS
London Chest ADL	33.8 (12.9)	33.7 (12.8)	NS
Nottingham Extended ADL	13.3 (4.5)	14.5 (4.5)	NS
HADa	8.4 (5.2)	6.9 (3.7)	NS
HADd	8.4 (3.7)	5.9 (3.5)	<0.05
DP % time weight bearing [n=9]*	22.7 [18.4-35.3]	31.0 [15.0-33.0]	NS
DP % time active [n=16]*	9.8 [6.5-12.0]	12.6 [8.9-14.7]	<0.05
DP % time walking [n=11]*	3.7 [2.0-4.5]	4.0 [2.8-6.9]	<0.05

*Median [interquartile range]

6.3.5 Changes in physical activity through the course of pulmonary rehabilitation

12 subjects completed assessment 2, which involved wearing DP after 4 weeks of PR. Table 7.4 summarises the measures of physical activity for patients who completed all 3 of the first assessments (before, 4 weeks and just after completing PR). Although we demonstrated significant changes in % time active and % time walking when comparing subjects pre and post PR (table 6.3), the statistical significance is lost when assessment 2 is included in a

smaller number of subjects, although the trends are still present. Although the numbers of subjects analysed are small, it appears that the greatest improvements in % time weightbearing and walking take place in the first 4 weeks of PR, with a slight decline over the rest of the course, while there appears to be a more steady increase in % time active (which includes lower limb and trunk activity) over the whole course of PR. Examination of the individual measures of physical activity at each visit (figures 6.2-6.4) demonstrates that there is variation between individuals, where subjects who continue to improve physical activity between assessments 2 and 3 are balanced by those who demonstrate decline. Two subjects showed dramatic improvement in % time weight bearing between assessment 1 and 2, followed by similarly dramatic decline between assessment 2 and 3 (figure 6.2); this may reflect regression to the mean.

Table 6.4: Physical Activity levels before pulmonary rehabilitation (assessment 1), after 4 weeks (assessment 2), just after pulmonary rehabilitation (assessment 3)

Median [interquartile range]	Assessment 1	Assessment 2	Assessment 3	p value
% time weight bearing [n=7]	27.8 [20.1-35.3]	34.5 [24.5-40.0]	33.0 [23.7-36.9]	NS
% time active [n=9]	10.1 [8.0-15.3]	11.9 [9.4-12.8]	12.5 [8.9-15.9]	NS
% time walking [n=6]	4.5 [2.9-6.8]	5.5 [4.8-7.5]	6.0 [3.6-7.9]	NS

Figure 6.2: Changes in % time weightbearing at each assessment through the course of pulmonary rehabilitation (1:before PR, 2:after 4 weeks, 3:end of PR)

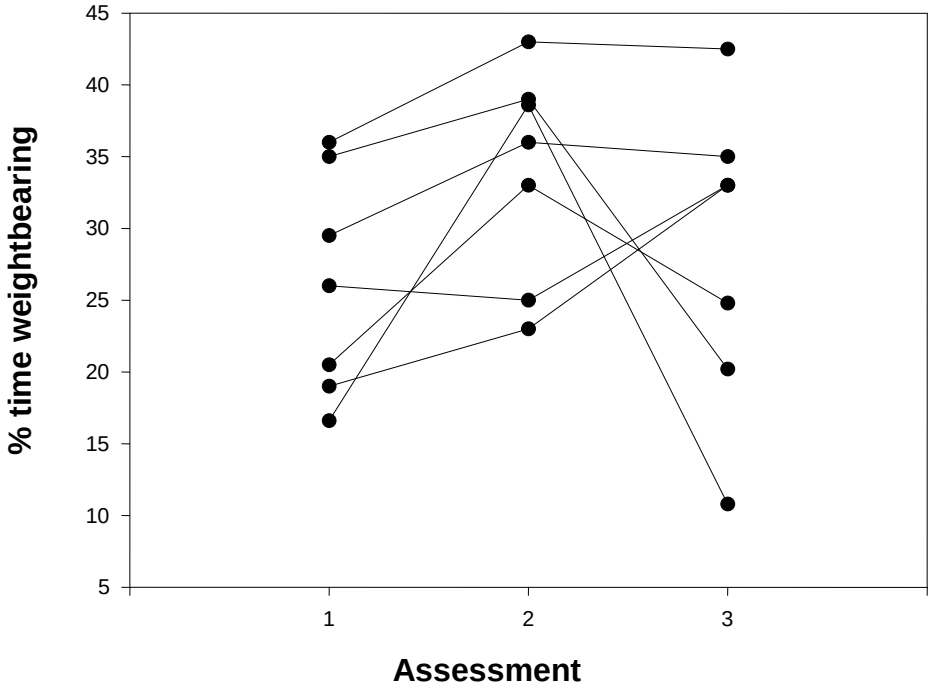


Figure 6.3: Changes in % time active at each assessment through the course of pulmonary rehabilitation (1:before PR, 2:after 4 weeks, 3:end of PR)

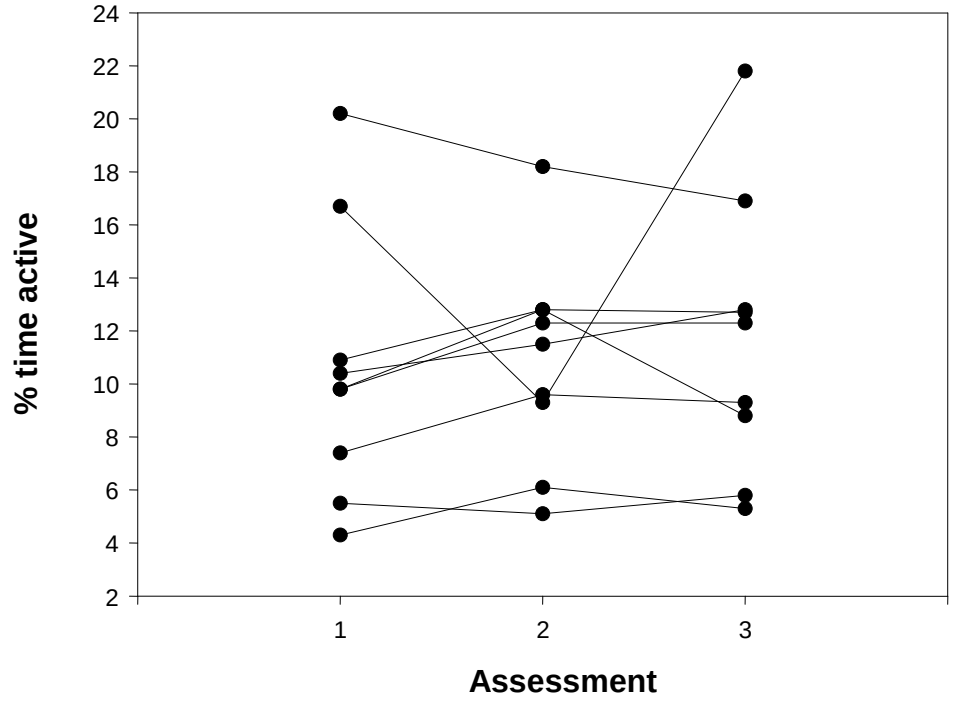
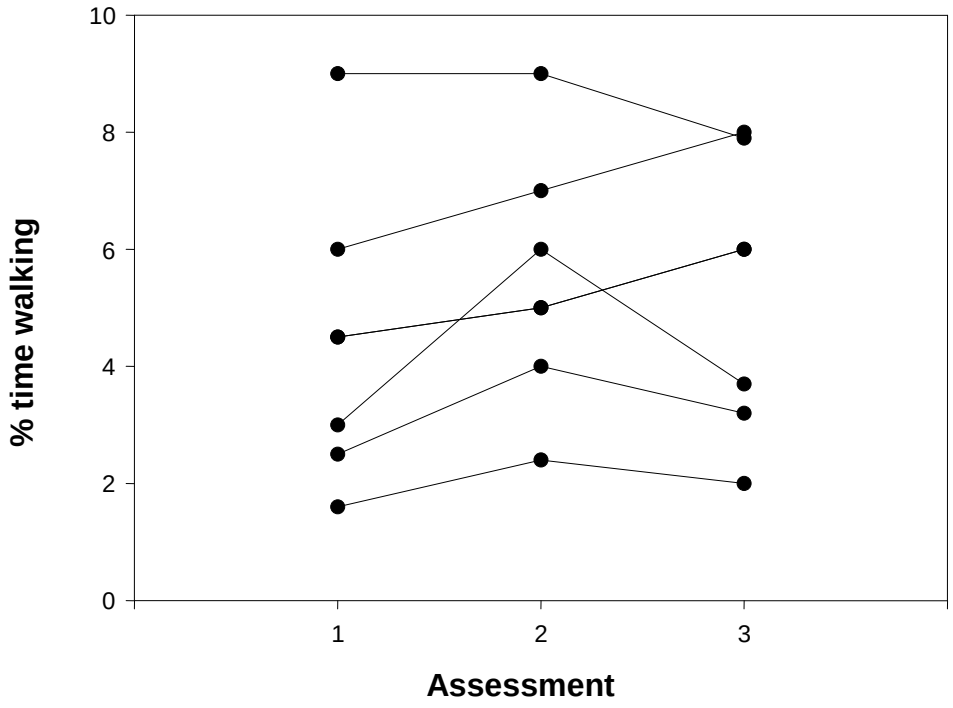


Figure 6.4: Changes in % time walking at each assessment through the course of pulmonary rehabilitation (1:before PR, 2:after 4 weeks, 3:end of PR)



6.3.6 Changes in physical activity and relationships with other measures

Although there was an overall increase in levels of physical activity following PR, not all patients achieved this. 2/7 patients decreased % time weightbearing, 3/13 decreased % time active and 3/8 decreased % time walking following the PR course (Table 6.5).

Table 6.5: Number of subjects who increased or decreased physical activity after completing pulmonary rehabilitation

Number	Increase	Decrease	No Change
DP % time weight bearing	7	2	0
DP % time active	13	3	0
DP % time walking	8	3	0

Table 6.6 illustrates the relationships between change in physical activity after PR and changes in other variables, and figures a-j are scatterplots illustrating these relationships. The

changes in all parameters were Normally distributed with the exception of change in ESWT, which was Normally distributed after logarithmic transformation. Since multiple analyses were made, a p value < 0.01 was accepted as significant.

Table 6.6: Correlations of changes in physical activity after pulmonary rehabilitation with changes in quadriceps force, exercise capacity and questionnaire scores

	Change QF	Log change ESWT	change SGRQ ACTIVITY	Change SGRQ TOTAL	Change HAD ANXIETY	Change HAD DEPRESSION	Change LCADL
Change % time weight-bearing	r= -0.10 NS	r= 0.24 NS	r= -0.27 NS	r= -0.39 NS	r= 0.45 NS	r= 0.46 NS	r= 0.39 NS
Change % time active	r= 0.07 NS	**r= 0.73 p<0.01**	r= 0.21 NS	r= -0.41 NS	**r= 0.65 p<0.01**	r= 0.53 NS	r= 0.12 NS
Change % time walking	r= 0.00 NS	r= 0.52 NS	r= 0.37 NS	r= -0.25 NS	r= 0.42 NS	r= 0.38 NS	r= 0.08 NS

There was a significant correlation between log change in shuttle walk and change in % time active (figure 6.5), but not with % time weightbearing or walking. Change in quadriceps force did not correlate with change in physical activity. Neither change in SGRQ (activity and total) nor change in LCADL correlated with any feature of physical activity. Surprisingly, there was a significant relationship between worsened HAD anxiety score and increased % time active (r= 0.65, p<0.01: figure 6.6) and a trend towards a relationship between worsened HAD depression score and increased % time active, although this was not statistically significant (R= 0.53, p=0.04: figure 6.7). On examination of the scatterplots, it seems that these data have been skewed by the 2 outliers who recorded very large falls in both HAD score and levels of physical activity.

Figure 6.5: Relationship between log change in ESWT distance and change in % time active between assessments 1 (pre PR) and 3 (post PR)

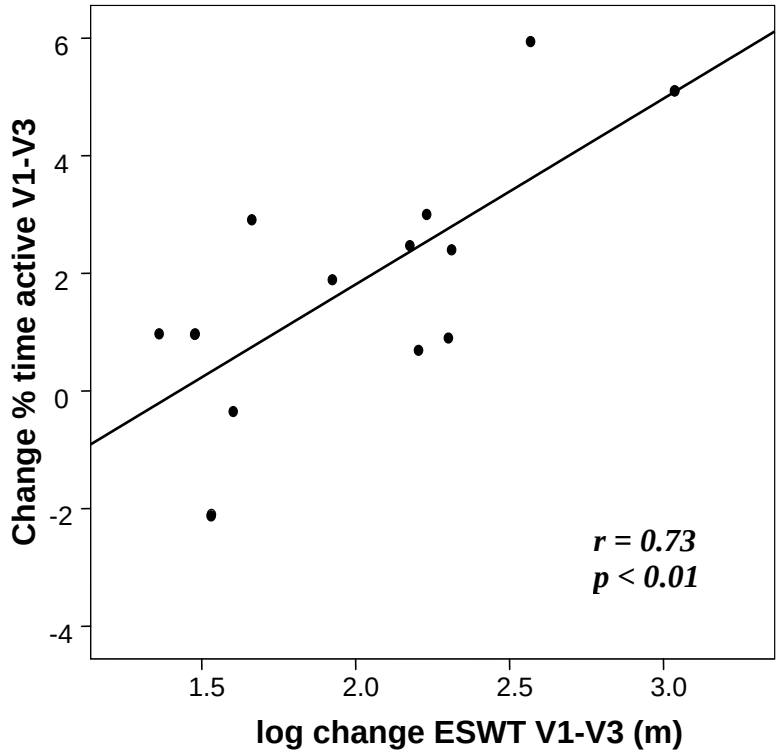


Figure 6.6: Relationship between change in HADa and change in % time active between assessments 1 (pre PR) and 3 (post PR)

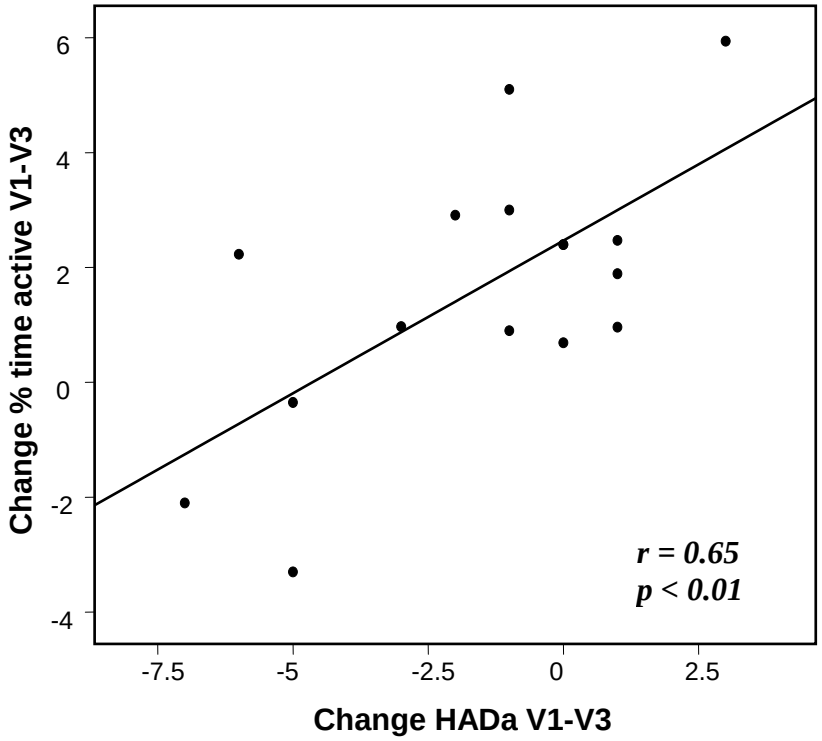
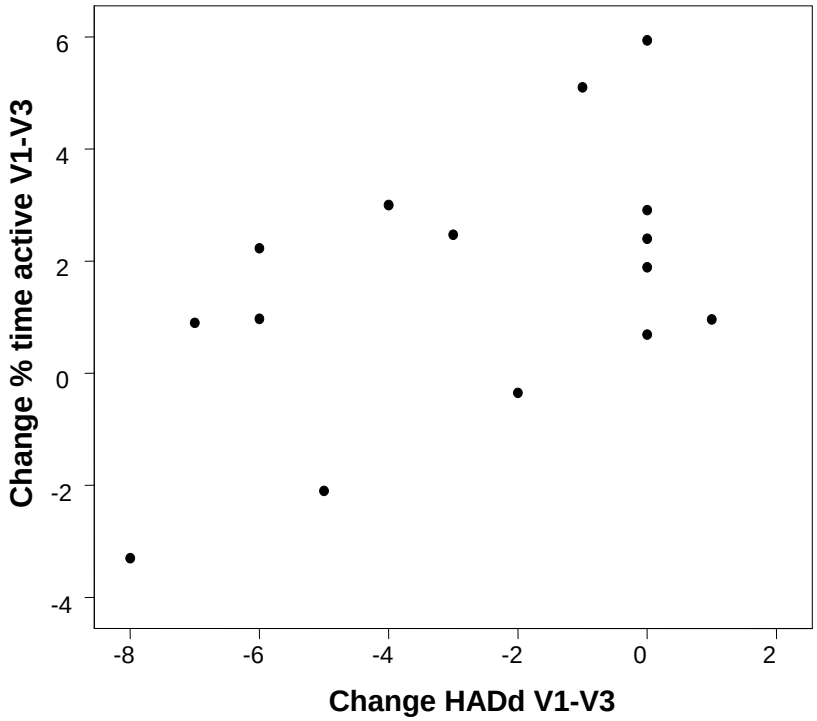


Figure 6.7: Relationship between change in HADd and change in % time active between assessments 1 (pre PR) and 3 (post PR)



6.3.7 Assessment of subjects 6 months after completing pulmonary rehabilitation

Table 6.7 demonstrates the characteristics of the 14 subjects who completed assessments 1 (pre PR), 3 (post PR) and 4 (6 months post PR), while figures 6.8-6.22 demonstrate the individual measures at each assessment, along with error bars with confidence intervals for the subjects collectively (box-whisker plots for non parametric variables). Although FEV_1 was stable, the decline in FVC absolute and % predicted after finishing PR continued over the subsequent 6 months, although this may have been largely due to 3 individuals who showed large drops in these readings (figure 6.8). While fat free mass was largely static over the 3 assessments, there was a trend towards improved quadriceps force, which was sustained 6 months later, although the level of statistical significance was not reached in these 14 patients when adjustment for multiple comparisons was made; there was considerable variation, with 6 subjects showing increase in QF 6 months after PR and 8 subjects showing a decrease

(figure 6.9). The improvement in ESWT was reasonably preserved 6 months later, although there was a small non significant decline in the median distance. The individual data showed wide variation: 2 subjects showed massive improvements in ESWT after PR, with one subject maintaining this, but the other subject subsequently declining to the pre PR level. Among the other subjects, the improvements post PR were more modest, with similar numbers showing either further improvement or subsequent decline in ESWT over the next 6 months (figure 6.10). SGRQ and its components showed very little change after PR, a result of similar numbers of subjects showing increase as those showing decrease (figure 6.11, 6.12). However, over the next 6 months, most subjects showed increase in SGRQ, and this was statistically significant for $SGRQ_{TOTAL.}$ The trends towards improvement in the CRQ fatigue, emotion and mastery domains straight after PR were small, a result of some subjects showing falls: half the subjects showed increase in CRQ dyspnoea score and half showed decrease, resulting in no overall change after PR. In the 6 months following PR, any increases in CRQ were generally then lost, with subjects back at pre PR levels (Figure 6.13-6.16). LCADL score, which was largely unchanged after PR (again, a balance of increases and decreases), subsequently increased over the next 6 months, and was significantly worse 6 months after finishing than it was before commencing PR (figure 6.17). A pronounced decrease followed by increase was seen for HAD anxiety and depression scores, with statistically significant improvement in HAD depression after PR: the majority of subjects demonstrated this pattern (figure 6.18, 6.19). The improvements that were seen in % time active and walking after PR (Table 6.3) lost statistical significance when adjustment for multiple comparisons was made in the smaller number of patients who completed the assessments 1, 3 and 4, although the trends in improvement in all 3 modalities of physical activity were still present. However, this was subsequently lost in the 6 months following PR completion, with statistically significant drops in % time weight bearing and active between assessments 3 and 4. On examination of

the individual data, the majority of subjects demonstrated improvement in all 3 modalities of physical activity after PR, followed by decline over the subsequent 6 months (figures 6.20-6.22).

Table 6.7: Characteristics of subjects before pulmonary rehabilitation (assessment 1), after finishing pulmonary rehabilitation (assessment 3), and 6 months later (assessment 4)

Mean (sd)	Assessment 1	Assessment 3	Assessment 4	p value
FEV_1 (l)	1.2 (0.4)	1.2 (0.5)	1.1 (0.4)	NS
FEV_1 % predicted	47.5 (17.8)	46.4 (19.9)	46.4 (21.4)	NS
FVC (l)$^{\Phi}$	2.6 [2.2-3.4]	2.5 [2.2-3.1]	2.2 [1.8-2.9]	<0.05*
FVC % predicted	83.2 (15.6)	75.9 (20.4)	71.8 (20.0)	<0.05*
FFM (kg)	49.5 (8.8)	49.2 (8.0)	48.8 (7.6)	NS
QF (kg) $^{\Phi}$	27.5 [21.9-30.6]	30.8 [23.8-36.0]	31.6 [21.2-39.6]	NS
ESWT distance (m) $^{\Phi}$	130 [42-175]	280 [101-395]	180 [90-375]	<0.05▪
$SGRQ_{SYMPTOMS}$ $^{\Phi}$	76.7 [58.7-85.0]	80.3 [53.3-93.4]	87.0 [69.4-91.4]	NS
$SGRQ_{ACTIVITY}$ $^{\Phi}$	84.9 [77.5-87.6]	82.1 [69.5-87.6]	85.9 [77.5-92.5]	NS
$SGRQ_{IMPACT}$	51.3 (17.8)	49.7 (23.5)	54.4 (20.6)	NS
$SGRQ_{TOTAL}$	63.7 (13.7)	62.5 (19.0)	67.3 (16.5)	<0.05♦
MRC $^{\Phi}$	4 [4-5]	4 [4-5]	5 [3.75-5]	NS
$CRQ_{DYSPNOEA}$	2.3 (1.2)	2.2 (1.1)	2.2 (0.8)	NS
$CRQ_{FATIGUE}$	3.4 (1.5)	3.7 (1.5)	3.4 (1.6)	NS
$CRQ_{EMOTIONS}$	4.3 (1.5)	4.7 (1.4)	4.2 (1.4)	NS
$CRQ_{MASTERY}$	4.5 (1.3)	5.1 (1.3)	4.5 (1.6)	NS
London Chest ADL	31.7 (11.9)	33.3 (12.4)	39.0 (12.8)	<0.05*
HADa	8.6 (5.5)	6.8 (3.9)	8.1 (4.8)	NS
HADd	8.8 (3.7)	5.8 (3.7)	7.9 (3.9)	<0.05▪
DP % weight bearing $^{\Phi}$ [n=8]	23.7 [20.1-33.6]	32.3 [22.2-34.5]	20.6 [13.6-23.4]	<0.05♦
DP % time active $^{\Phi}$ [n=13]	10.5 [9.4-13.9]	12.8 [10.8-15.5]	11.9 [9.1-13.2]	<0.05♦
DP % time walking $^{\Phi}$ [n=9]	4.5 [2.8-5.9]	6.0 [3.9-7.9]	2.9 [2.3-5.3]	NS

$^{\Phi}$ Median [interquartile range]

* significant between assessment 1 and 4
▪ significant between assessment 1 and 3
♦ significant between assessment 3 and 4
(Bonferroni adjustment for multiple comparisons)

Figure 6.8: Changes in FVC (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with box-whisker plots

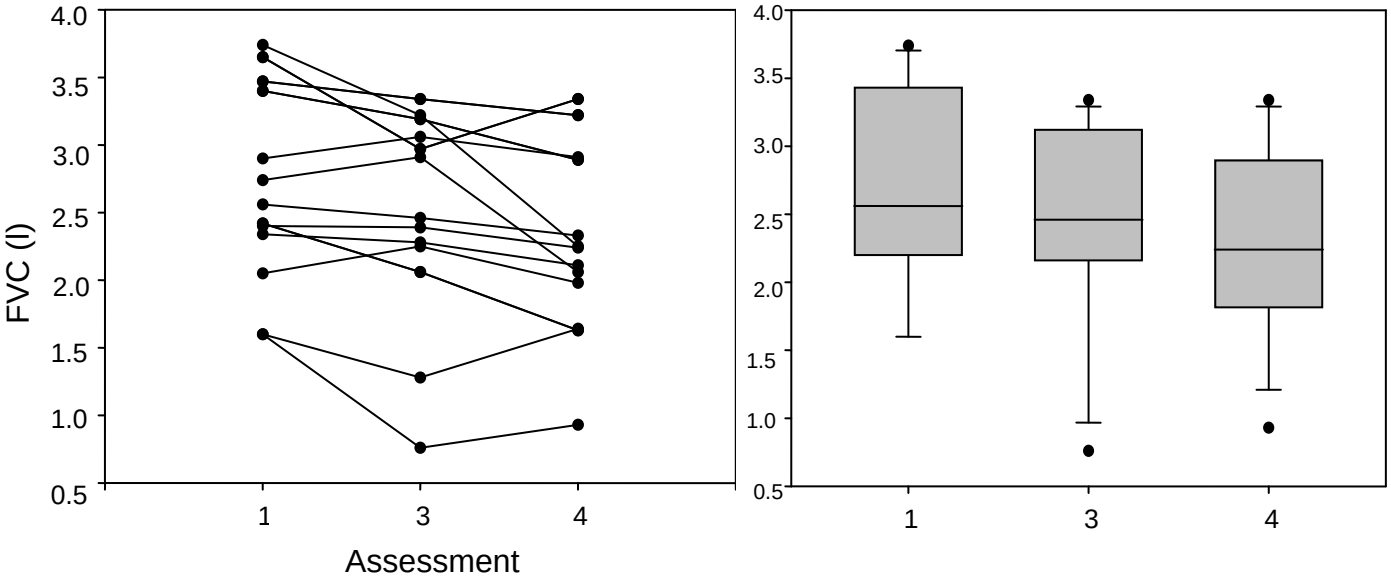


Figure 6.9: Changes in quadriceps force before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with box-whisker plots

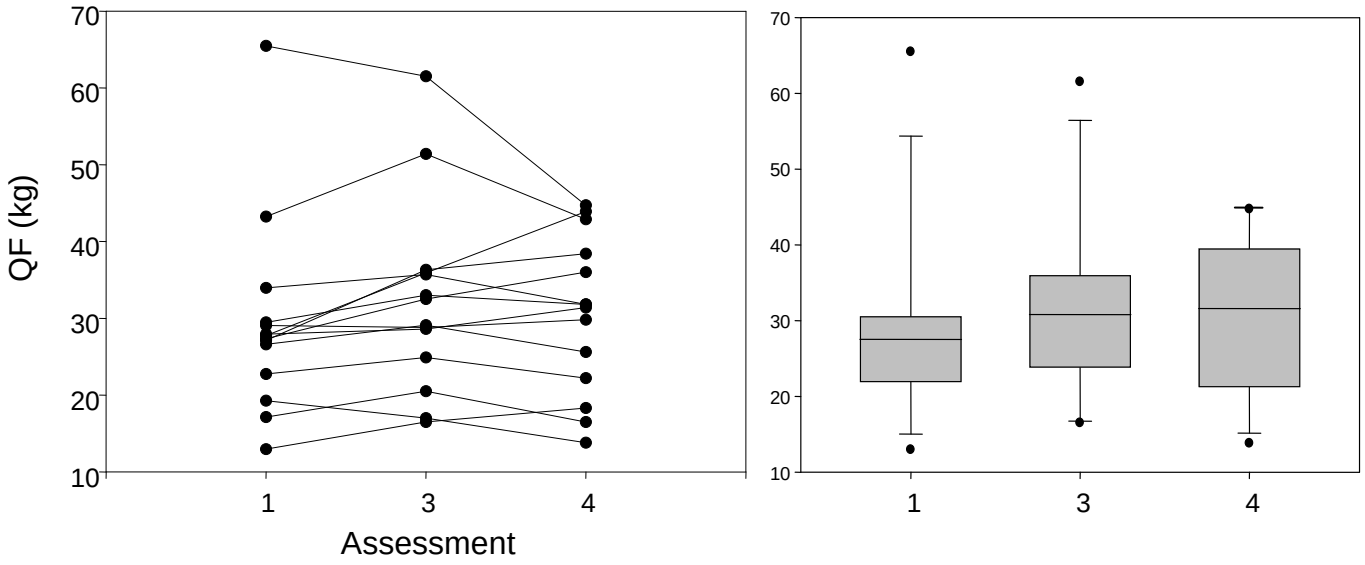


Figure 6.10: Changes in endurance shuttle walk distance before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with box-whisker plots

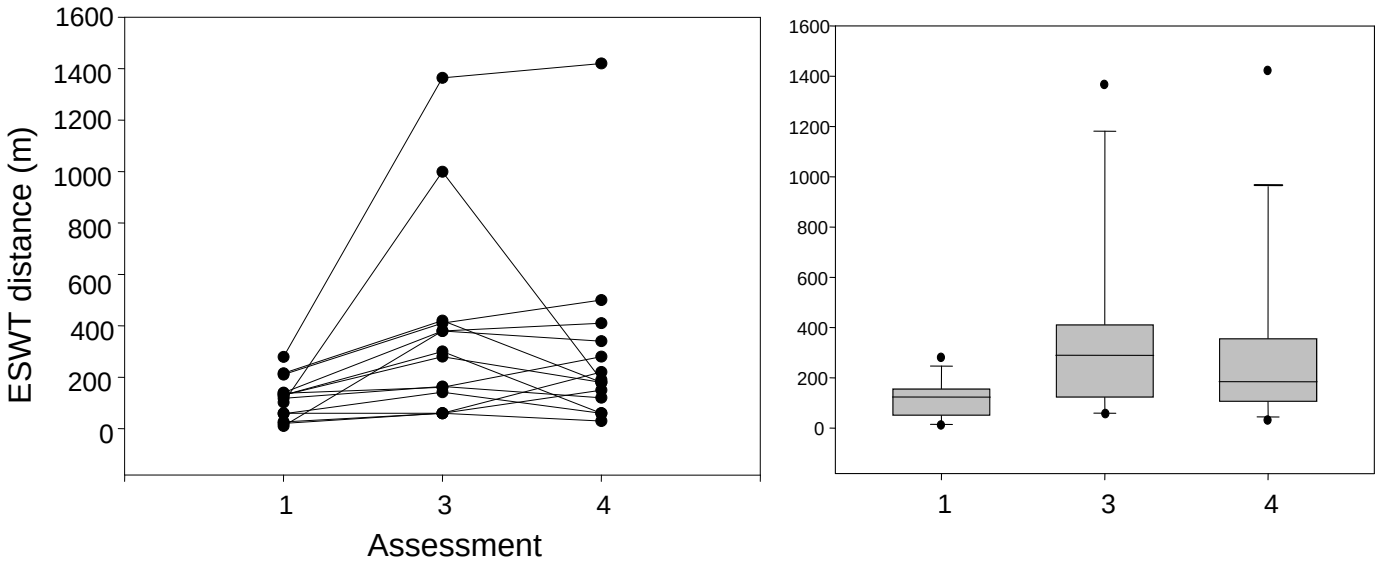


Figure 6.11: Changes in $SGRQ_{ACTIVITY}$ before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with box-whisker plots

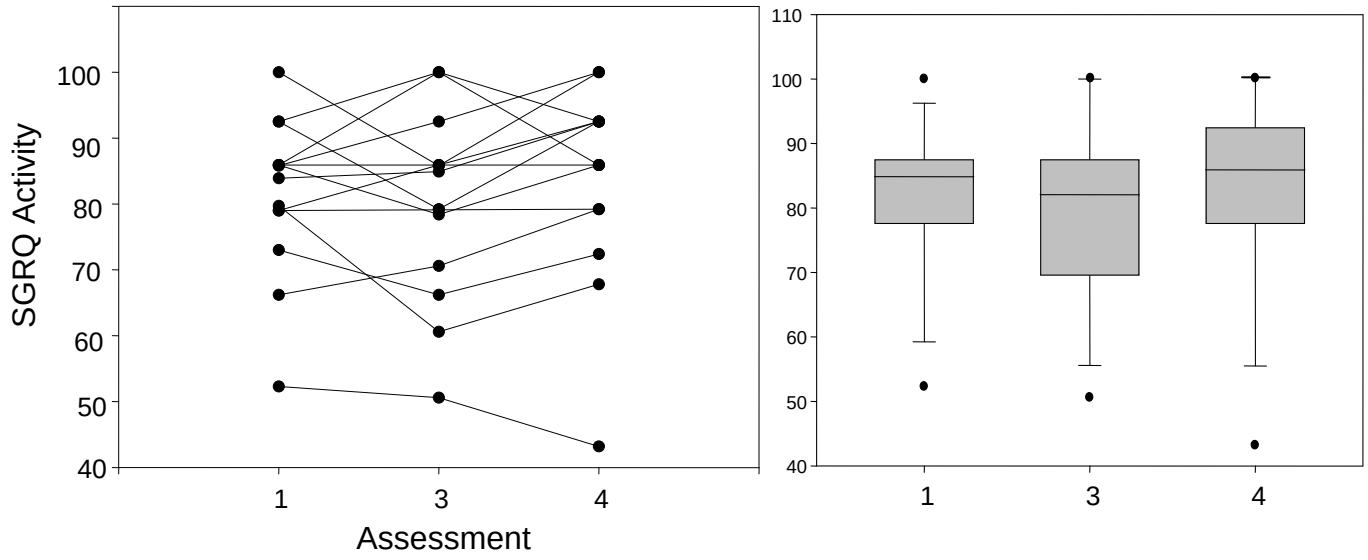


Figure 6.12: Changes in $SGRQ_{TOTAL}$ before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with error bars (95% CI)

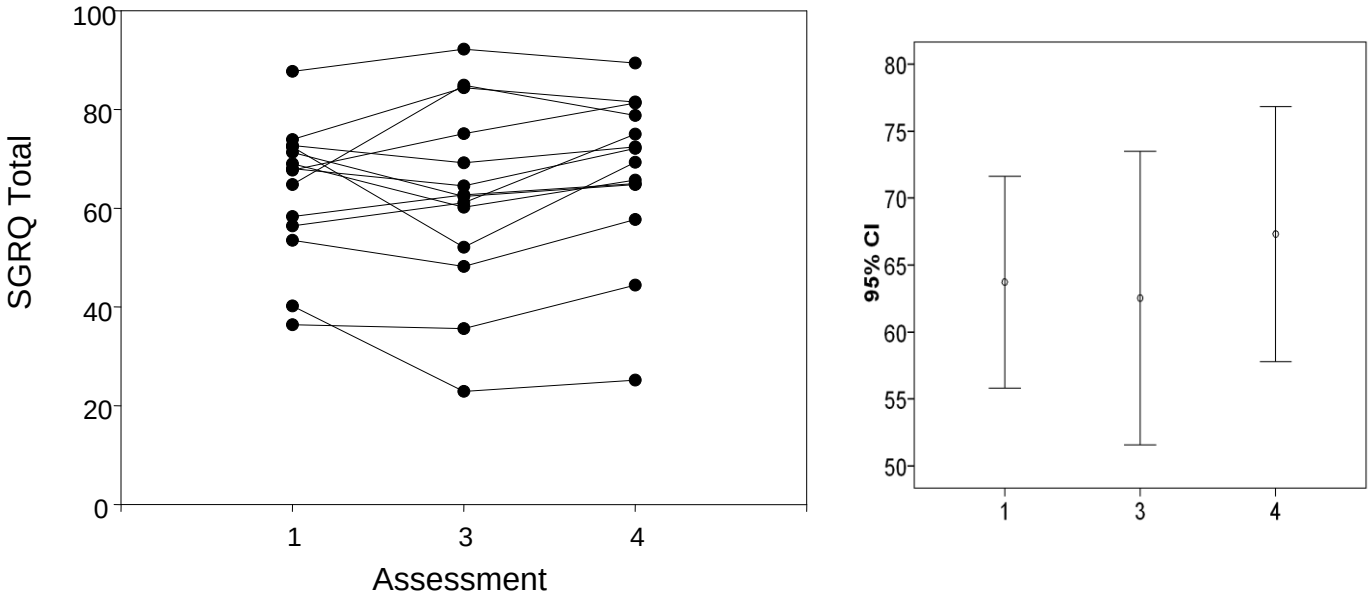


Figure 6.13: Changes in $CRQ_{DYSPNOEA}$ before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with error bars (95% CI)

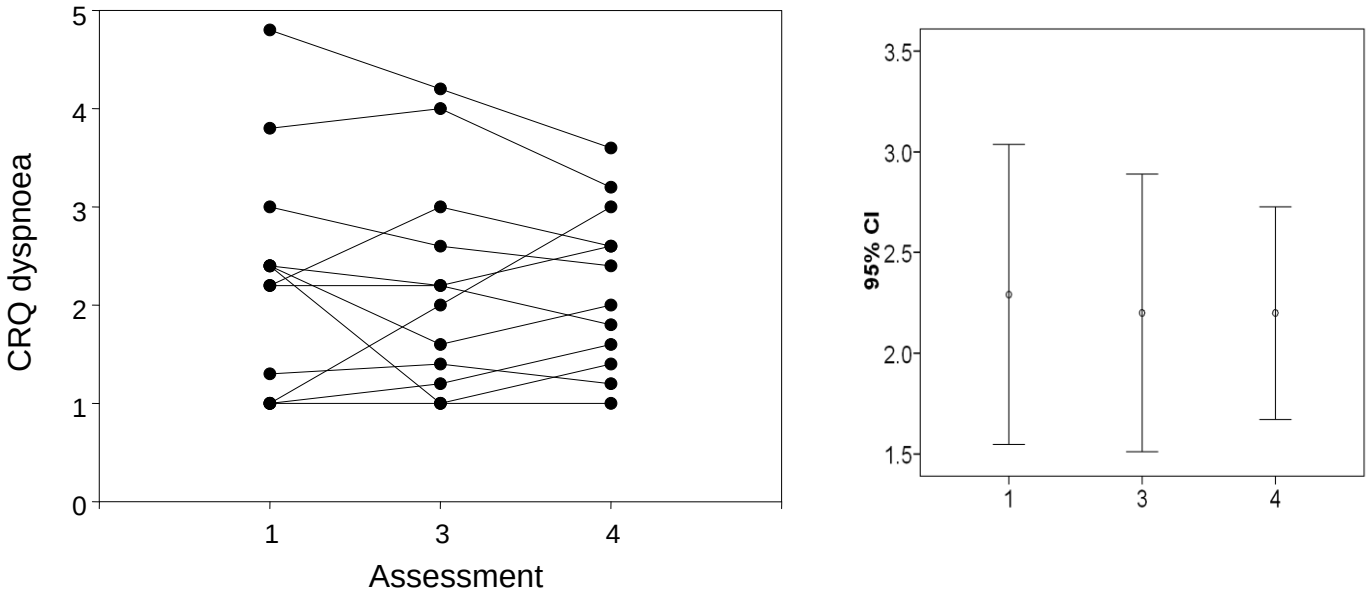


Figure 6.14: Changes in $CRQ_{FATIGUE}$ before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with error bars (95% CI)

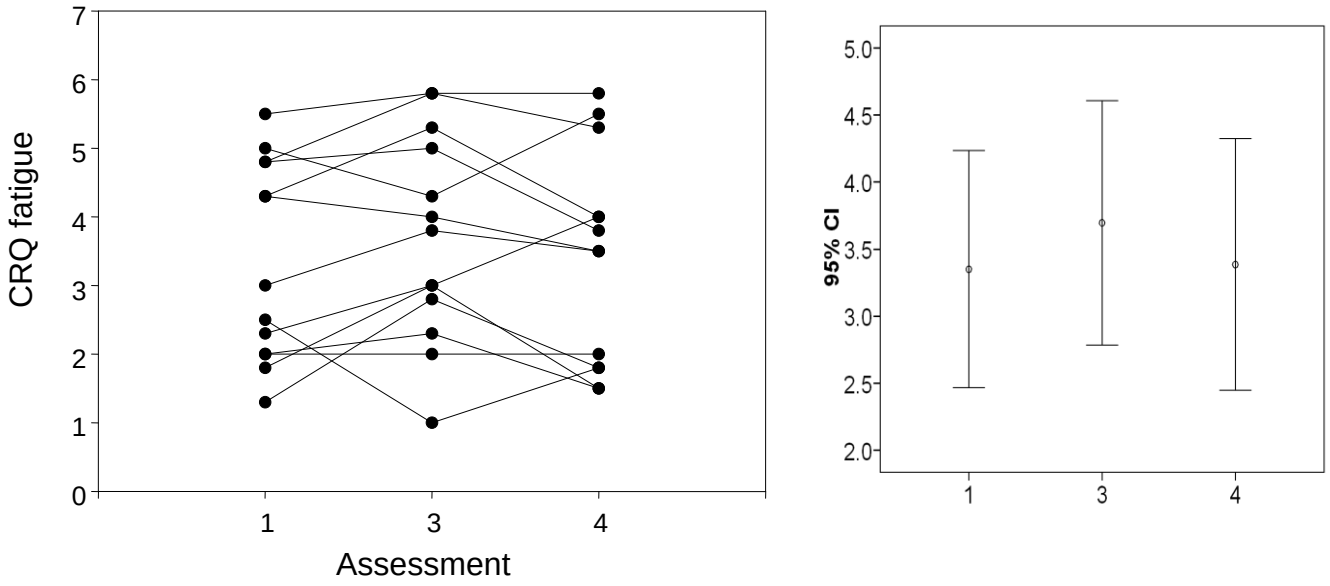


Figure 6.15: Changes in $CRQ_{EMOTION}$ before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with error bars (95% CI)

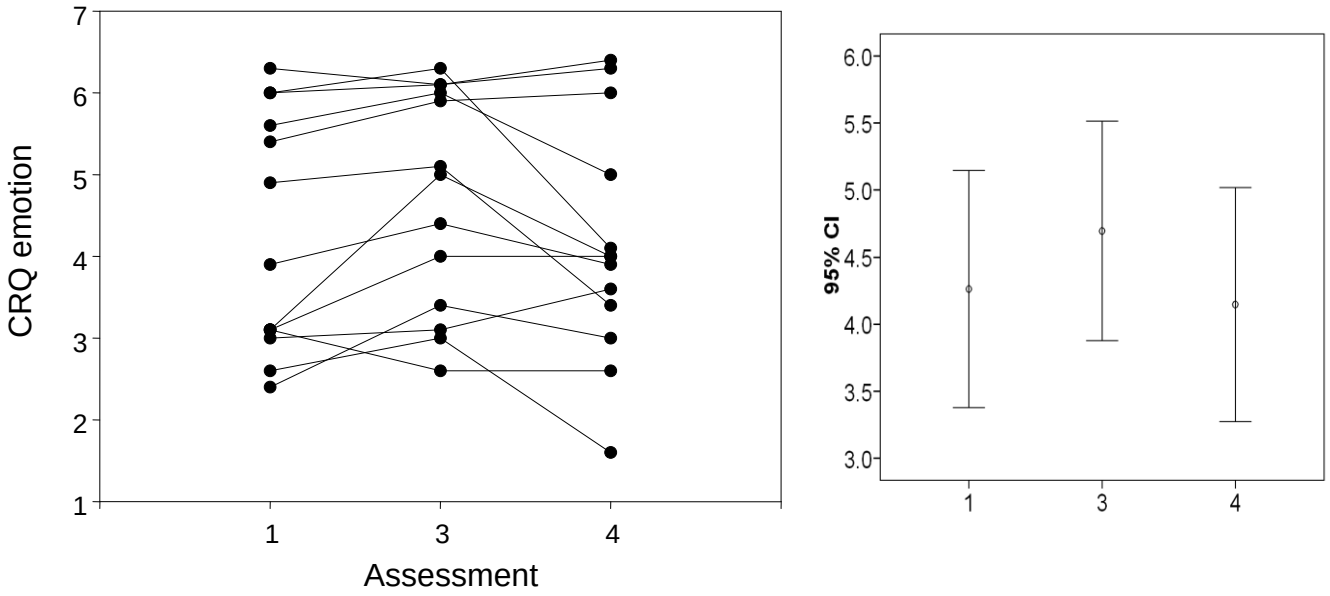


Figure 6.16: Changes in $CRQ_{MASTERY}$ before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with error bars (95% CI)

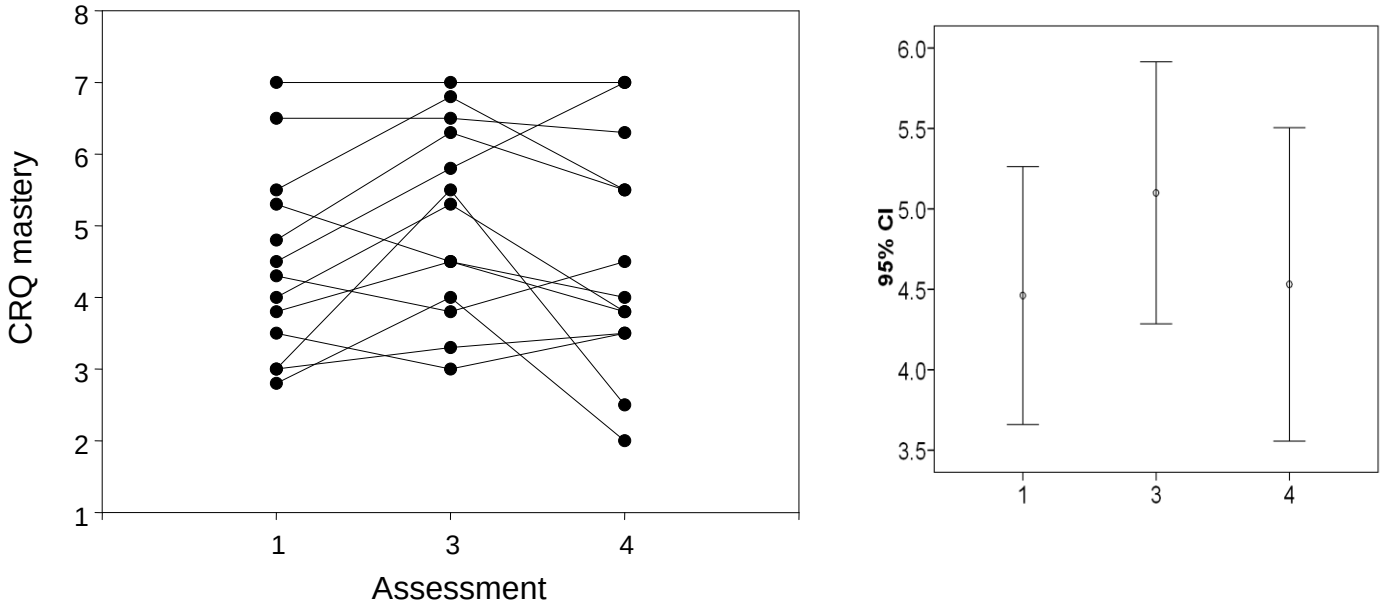


Figure 6.17: Changes in LCADL before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with error bars (95% CI)

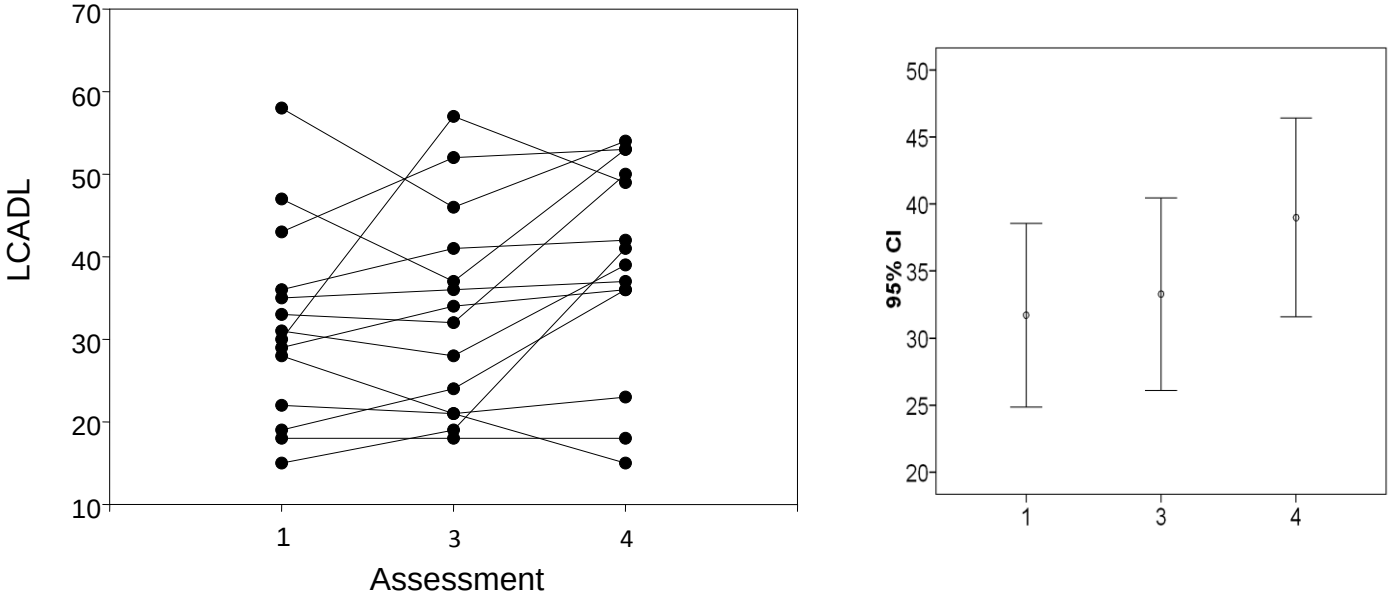


Figure 6.18: Changes in $HAD_{ANXIETY}$ before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with error bars (95% CI)

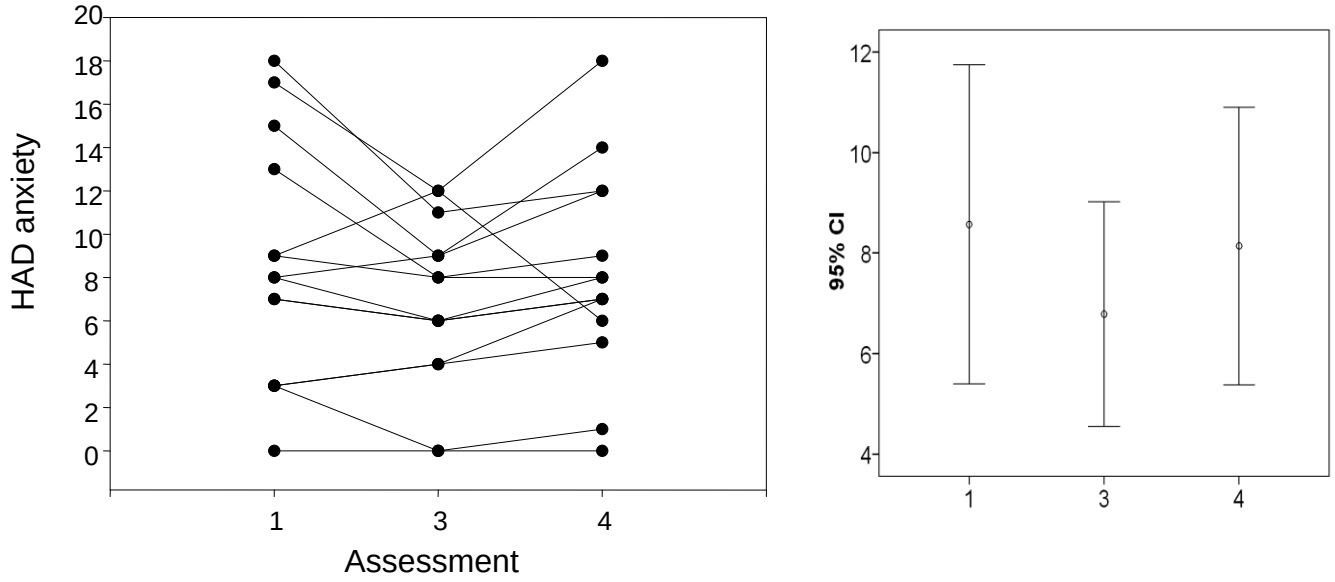


Figure 6.19: Changes in $HAD_{DEPRESSION}$ before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with error bars (95% CI)

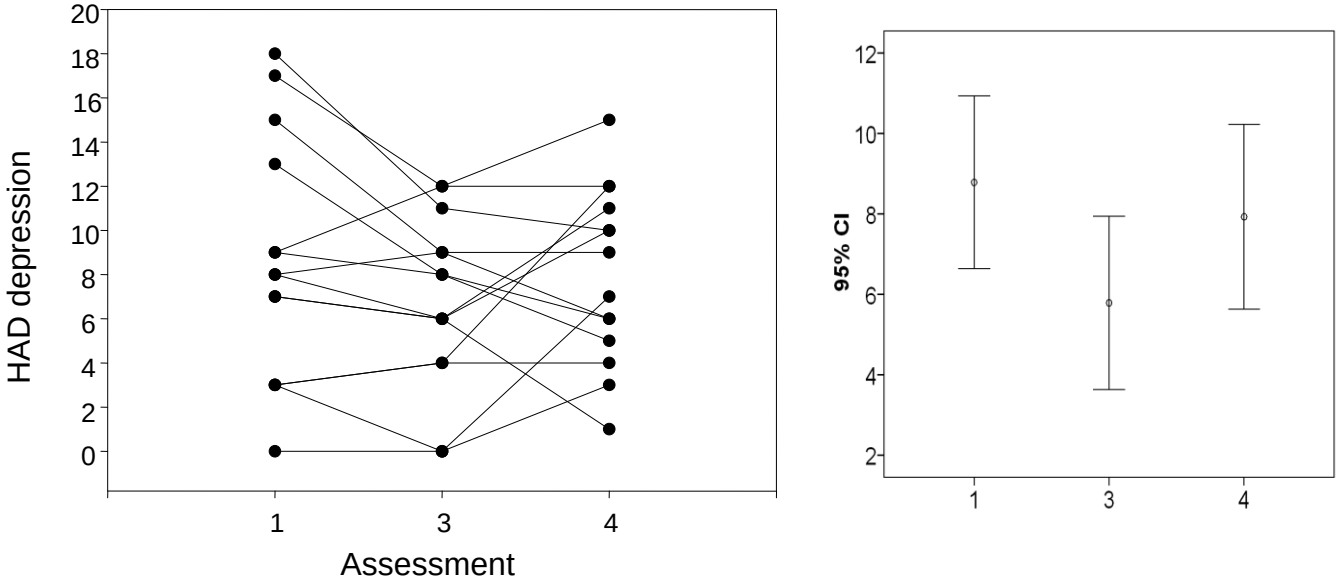


Figure 6.20: Changes in % time weightbearing before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with box-whisker plots

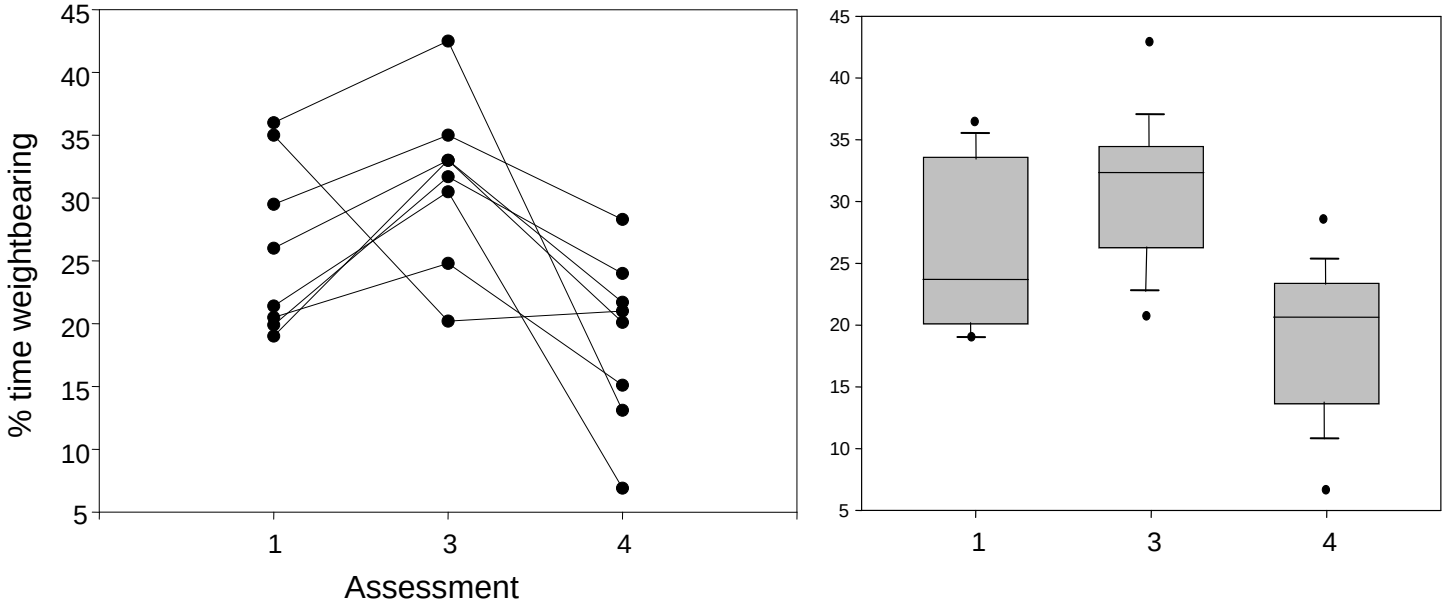


Figure 6.21: Changes in % time active before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with box-whisker plots

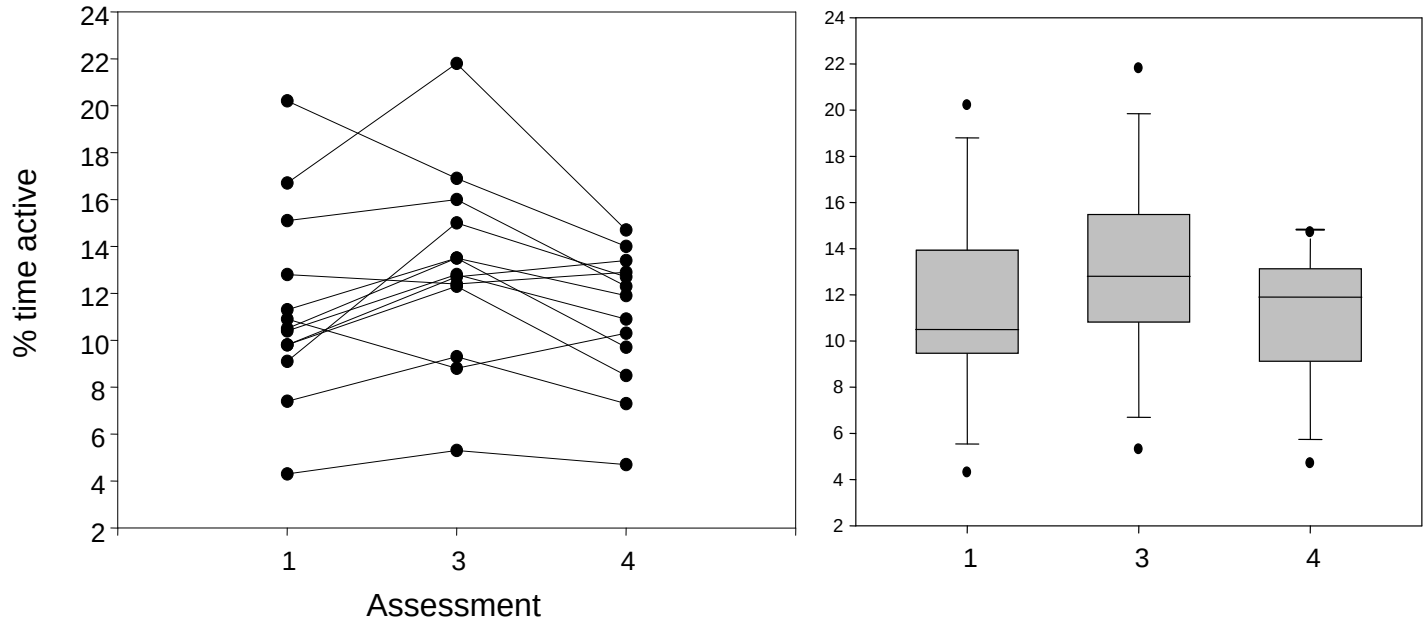
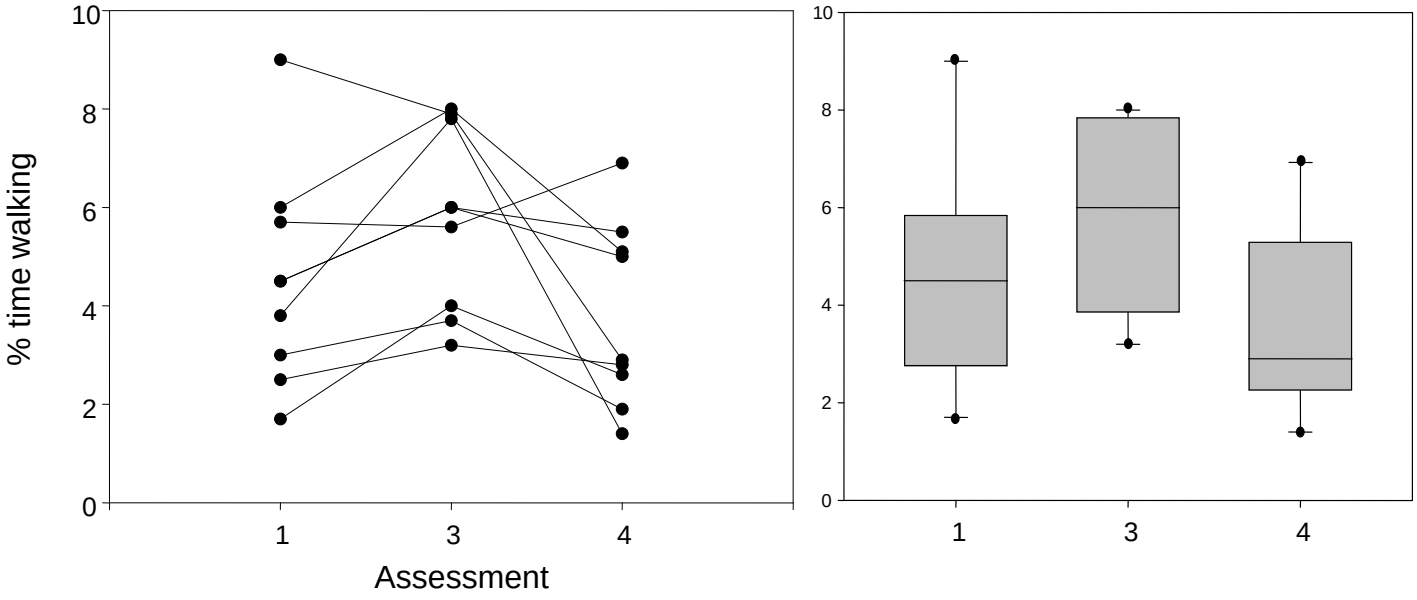


Figure 6.22: Changes in % time walking before (assessment 1), after (assessment 3) and 6 months after (assessment 4) pulmonary rehabilitation, with box-whisker plots



6.4 Discussion

Of 33 COPD patients in this study who started PR, 17 (52%) completed the course. Pulmonary hyperinflation was the only predictor of PR completion. Patients who completed the course of PR demonstrated significant improvements in levels of physical activity (% time active and % time walking). Subjects also demonstrated significant improvements in peripheral muscle strength, exercise capacity and depression scores, although changes in these measures were not related to changes in physical activity. Most of the improvements in physical activity seemed to occur by the time subjects were half way through the PR course, with a plateau over the second half, although there was considerable subject to subject variation. In the 6 months following PR, the improvements in depression scores and physical activity were subsequently lost. While this patient group failed to show a significant improvement in health related quality of life or self reported ability to carry out activities of

daily living, these measures significantly deteriorated in the 6 months following PR. While FEV_1 remained stable over the 3 assessments, FVC absolute and % predicted fell significantly, with a median loss of 400mls over this period. It is difficult to explain this and it may reflect suboptimal manoeuvres by a few individuals rather than a pathological process. Although we did not draw conclusions from the gas transfer analysis, we acknowledge that we did not correct for haemoglobin in our analysis, which will have resulted in inaccuracies for anaemic and polycythaemic patients.

The median MRC score in the patients was 4 before commencing PR. NICE Guidelines recommend that PR should be offered to subjects who consider themselves functionally disabled by COPD, usually MRC grade 3 or above (dyspnoeic walking at own pace or unable to keep up with contemporaries)(209). It may therefore be the case that PR has been provided too late to some of our patients for them to obtain maximum benefit, although it has been reported that COPD patients of all MRC grades gain comparable benefit post PR in terms of improved exercise capacity(210).

The 48% rate of failure to complete PR is higher than that in most other series, some with a much longer PR course (Troosters 6 months PR, 31% non completion(211); Pitta 6 months PR, 29% non completion(169); Cockram 8 weeks PR, 25% non completion(212), Walker 8 weeks PR, 27% non completion(166)). Fischer identified a 23% non completion rate among 217 COPD patients commencing a 12 week PR course. No baseline clinical, psychological or demographic variables predicted non completion(213). Cote identified a worse BODE score as a predictor for failure to take up or complete PR(214) while Young identified social isolation and smoking status as predictors(215). However, we assessed only patients who had already agreed to commence PR, and it is therefore difficult to make direct comparisons. The only factor that we identified as a predictor for non completion was RV/TLC ratio, with a trend towards lower baseline FEV_1, FVC and TLCO in the non completers. It is recognised

that PR does not impact on static lung physiology and it might therefore be the case that patients with more impaired lung function and pulmonary hyperinflation will be more breathless on carrying out the PR sessions without experiencing benefits, and this may lead to premature withdrawal from the PR course. Not all patients may have been on optimal pharmacotherapy before commencing PR, with 7 patients not receiving inhaled long acting antimuscarinic agents. This may in part explain why some of our post-PR outcomes were not as good as one might expect (216). The large decline in FVC in subjects who do complete PR is much greater than the decline in FVC of approximately 60ml/year that is usually recognised in COPD(217) and is difficult to explain, although this may be due to suboptimal manoeuvres by a few individuals.

Pitta assessed changes in physical activity with the DynaPort in 29 subjects with comparable age, spirometry and quadriceps force after a 6 month course of PR (3 times weekly for the first 3 months, then twice weekly)(169). Health status was slightly better in Pitta's subjects than subjects in this study at baseline ($CRQ_{DYSPNOEA}$ 2.8 vs 2.3; $CRQ_{FATIGUE}$ 3.8 vs 3.3). Pitta's subjects spent 39.2% of the time in weightbearing activities and 7.6% of the time walking at baseline in comparison to 22.7% weightbearing and 3.7% walking in this patient group. This suggests that our patients were less active than Pitta's to start with, although it should be borne in mind that Pitta's patients were assessed over a 12 hour day, whereas subjects in our study were assessed from waking until bedtime, which was usually longer than 12 hours and included late evenings when activity is generally reduced(218). Pitta's patients improved % time walking to 8.2% after 3 months' PR ($p>0.05$) and 9.0% after 6 months' PR ($p<0.05$). This contrasts with a smaller but statistically significant increase in median % time walking from 3.7% to 4.0% after 8 weeks' PR in our study. Pitta reported that improvements in physical activity after PR could not be predicted by any variable with the exception of change in CRQ. We found that improvement in exercise capacity was related to

improvement in % time active, but that improvement in anxiety was related to decline in % time active, although this paradoxical finding was probably caused by 2 outliers. We did not identify any other variable that predicted change in physical activity including CRQ, but this variable did not significantly improve in our subjects in contrast to those in Pitta's group.

A limitation of this study is the small number of subjects that managed all assessments. Some subjects demonstrated significant changes between visits, sometimes declines after PR, particularly with respect to measures of physical activity. This might be reflective of day to day variability with the DynaPort readings and it is possible that readings over 2 consecutive days did not yield stable data for some subjects. However, many patients found the DP cumbersome and uncomfortable to wear, so may have been reluctant to wear it for more than 2 days. Moreover, assessment 2 needed to take place on days when PR was not taking place, which provided only a 2 day window in many cases. Pitta has previously reported that 2 days' assessment with DP is sufficient to provide an acceptable intra-class reliability coefficient(167). The data from assessment 2 also offers assurance that subjects maintain physical activity on non-PR days while undertaking a course of PR and don't treat them as rest days. A further limitation is that limited availability of monitors meant that it was not always possible for subjects to wear the same activity monitor at each assessment. This may have affected the variability in individual data from assessment to assessment, but it will not have affected the measures of group data. There is probably an element of selection bias among the COPD patients in this study: they had already agreed to take part in a course of PR at the time of first assessment, and were also willing to enter a study entailing additional assessments. It is therefore likely that we have studied a more motivated group of patients than the general population of COPD subjects who are referred for PR.

Although we have probably studied a more motivated patient group than our general COPD population, these patients commenced PR with a poor health status (mean $SGRQ_{TOTAL}$ 65.6).

This is much worse than the baseline $SGRQ_{TOTAL}$ score in some other PR studies (Coronado: 42.0(206), Spencer: 43.0(219)). Although it might be expected that these patients are those who stand to gain the most from PR, we have reported a very high non completion rate, and no improvement in health status following PR. This raises the possibility of this being a static patient group with a health status that is resistant to change. However, these patients did demonstrate improvement in muscle strength, exercise capacity and depression scores after PR, in addition to improved physical activity. Moreover, the baseline $SGRQ_{TOTAL}$ is similar to Griffiths' subjects (mean baseline score 64.9, with a change of -7.1 after 6 weeks' PR(125)) and not much worse than Walker's patients (mean score 62.9) at baseline, in whom a large improvement (mean change -15.1) was seen after a similar course of PR in patients recruited from the same geographical population(166). Since only 2 of the patients who completed assessment 3 were from the Litherland community programme, it was not possible to assess if outcomes were different in the hospital versus community based service.

While we demonstrated an increase in exercise capacity with PR in keeping with most previous studies, patients in our study had a lower ESWT distance than Sewell's group (baseline 102m vs 238m; post PR 172m vs 749m) despite better FEV_1(170) and comparable health status. This also contrasts with Dodd's study in patients with comparable FEV_1 and age but better baseline health status, in whom ESWT increased from 294m to 502m after PR(220). However, our patients as a group achieved the 60-115m minimal important difference that has been suggested as likely to be perceived by patients after bronchodilation(221). Direct comparison with other studies is not possible since the 6 minute walk distance was normally used.

The improvement in physical activity that we have demonstrated after 8 weeks' PR is consistent with Walker's findings with the uniaxial Actiwatch accelerometer (worn on the leg) after 8 weeks' PR(166) and Sewell's findings with the uniaxial Z80-32k device (worn at

the waist) after 7 weeks' PR(170). Pitta used the same triaxial device as us to demonstrate significantly increased % time walking after 6 months' PR(169). Additionally we demonstrated significantly increased % time active, which includes whole body movement and low level activity, after 8 weeks' PR. Although we found a trend towards increased % time in weightbearing activity after PR, this did not reach levels of statistical significance: it is possible that some subjects who are increasing the amount of time walking are doing so at the expense of the time standing rather than sitting or lying. However, in view of the small number of subjects, it is difficult to make firm conclusions.

Dallas, using a pedometer (worn at the waist) in 45 COPD patients, did not find a significant improvement in hourly step count after PR, although there was a significant increase when only the 50% of subjects with lower baseline activity were analysed. The length of the PR course varied between individuals in this study from 6-12 weeks(207). Steele, using the Tritrac R3D triaxial accelerometer worn at the waist in 38 subjects, found no significant change in activity count after 8 weeks' PR(171). Coronado studied 15 COPD patients during a 3 week inpatient PR course using the SCAM uniaxial accelerometer worn over the lower lumbar spine(206). There was no significant difference in % time inactive, in low activity or in medium activity at the end of the PR course when the activity carried out during the PR sessions themselves was excluded. However, the data were based on a single day's recording at the start of the PR being compared with a single reading on the last day of the course, and therefore cannot account for day to day variation. Additionally, subjects were still in the environment of the rehabilitation centre when the readings were made rather than in the home environment where other studies (including ours) have based the readings. Of note, these 3 negative studies involved the activity monitor being worn at the waist or lower back. Given Walker's finding that lower limb activity is the main determinant of whole body activity in

COPD patients(166), it may be the case that activity monitors placed solely on the trunk are less sensitive at detecting the increased activity levels that result from PR.

While we have demonstrated significant improvements in peripheral muscle strength, exercise capacity and depression scores (and trends towards increased physical activity when adjusting for multiple comparisons) after PR, some of these benefits are lost 6 months later. This contrasts with previous studies demonstrating that the benefits of PR (improved exercise capacity dyspnoea and health status) last for longer.

Cambach's metanalysis of COPD and asthmatic patients found that the improvements in exercise capacity last up to 9 months after PR(127). Griffiths found that, although the improvements in exercise capacity and health status declined after the end of 6 weeks' PR, they remained significantly better than baseline at 1 year's follow up(125). Singh showed maintenance of the improvements in exercise capacity and health status 10 months after 7 weeks' PR(222). Foglio found that the benefits in exercise capacity were lost 12 months after PR as were the improvements in health related quality of life in half of subjects(128). Bestall demonstrated decline in exercise capacity and health status towards baseline in the 12 months following 8 weeks' PR(126). In our patient group, while peripheral muscle strength and, to a lesser extent, exercise capacity are maintained 6 months after finishing 8 weeks' PR, the improvement in depression scores are lost, in addition to levels of physical activity, with a significant drop in % time weightbearing and active in the 6 months following PR. This is accompanied by a significant decline in health status (mean $SGRQ_{TOTAL}$ increase 4.8) while self reported ability to carry out activities of daily living declines and is significantly worse 6 months after finishing PR than it was before starting. This indicates that, in this patient group, most benefits of PR are lost earlier than that reported previously. The maintenance of quadriceps strength and exercise capacity, however, suggests that, while some of the physiological benefits of PR might persist, this has not translated into a sustained change in

patient behaviour. For real long term benefits of PR to be realised, it may be the case that embedding long term behaviour change is necessary: this is often difficult to achieve in many fields of health improvement, including smoking cessation and weight loss(223, 224).

Several studies have looked at ways of trying to sustain the benefits of PR. Troosters examined the effects of a prolonged PR course (high intensity 90 minute sessions delivered 3 times weekly for 3 months then twice weekly for 3 months) and reported sustained improvements in exercise capacity and quality of life 12 months after finishing the treatment(211). 31% of patients dropped out during the 6 month PR course, although this is better than our 48% drop out rate during an 8 week course. Berry reported a greater improvement in exercise capacity and self reported disability after 18 months when thrice weekly moderate intensity PR was delivered over 18 months compared with 3 months(129). Ries examined the effects of a 12 month maintenance programme, consisting of weekly telephone calls and monthly supervised reinforcement sessions after a standard 8 week PR course(130). While the control group showed decline in exercise tolerance and health status in the 12 months following initial PR, these were preserved in the treatment group, along with a modest reduction in healthcare utilisation. However, exercise capacity and quality of life declined in the second year of follow up (when no intervention was delivered to any subjects) towards pre-rehabilitation levels. A similar study by Brooks, entailing 12 months' enhanced follow up post PR with monthly exercise sessions and telephone calls, demonstrated no significant benefits in exercise capacity or health related quality of life at 1 year(225). Spencer compared 2 forms of maintenance PR delivered over 12 months after 8 weeks' standard PR. 24 patients received weekly supervised exercise in addition to unsupervised exercise on 4 other days per week and 24 patients carried out only unsupervised exercise 5 days per week. Both groups maintained health status and exercise capacity at 12 months with no significant difference between the 2 groups(219). These patients had milder

disease than subjects in many other studies including ours (FEV_1 57-60% predicted, pre-PR 6 minute walk distance 523-530m) and this may be a reason for the sustained improvements in this group. Steele reported that a largely home based exercise adherence programme delivered after PR showed modest short term improvements in exercise capacity and self reported physical activity (although this was not demonstrated objectively with accelerometers), but no long term benefits(132). A number of these studies included patients with chronic respiratory conditions, although the majority of subjects had COPD, so it is unlikely that a cohort of 'pure' COPD subjects would have altered the outcomes.

These studies show different outcomes since they look at different populations with different severity and, perhaps more importantly, deliver the PR in different ways. The intensity of the PR may be a relevant factor. Most PR programmes, including that in our study, are delivered at moderate intensity, with subjects encouraged to increase the intensity of the exercises as the programme progresses. Trooster's 6 month programme was delivered at high intensity, with subjects starting the programme at 60% of maximal workload, increased to 80% over 3 months(211). Similarly, it may be that self-delivered programmes require high intensity exercises if they are to be of benefit, as suggested by Liu's study of cell-phone paced endurance exercise training at home(226).

Our data suggest that, while some of the conventional benefits of PR are lost at 6 months, actual performance of daily physical activity also diminishes over this period of time. The importance of daily physical activity is well recognised, and reduced physical activity is a predictor of readmission for exacerbation(43, 77) and mortality(92). The fact that conventional pulmonary rehabilitation appears to confer only short term benefits in daily physical activity needs addressing. The preservation of peripheral muscle strength and, to a lesser extent, exercise capacity, suggests that patients retain the ability to carry out increased activity, but do not actually do so. Trying to alter patient behaviour in the long term therefore

seems to be important. While there is some evidence that prolonged or maintenance PR might confer health benefits, there is a lack of data to suggest that this includes sustained physical activity measured by accelerometry, and this is an important measure that should be included in future studies. It may be that COPD patients need a long term, possibly indefinite, programme of maintenance PR in order to sustain the benefits. The cost of delivering such programmes would be very high. Encouraging some healthcare providers to fund such schemes is likely to be a challenge, particularly when conventional PR is often under resourced and under delivered to some populations(227) despite its proven cost effectiveness(228).

Chapter 7: Physical activity in COPD patients assessed for long term oxygen therapy

7.1 Introduction

Long term oxygen therapy (LTOT) for severely hypoxaemic patients has been shown to reduce mortality in COPD. In the NOTT study, subjects with PaO2 < 7.9 kPa who received continuous oxygen at a flow rate of 1-4 l/min had improved mortality at 24 months in comparison with subjects who received only nocturnal oxygen; the benefits were even greater with continuous (24 hour) oxygen(105). In the MRC study, COPD patients with PaO2 5.3-8 kPa with at least one episode of heart failure were randomized to LTOT for at least 15 hours per day at a rate of at least 2 l/min, or no oxygen. The active group had significantly lower 5 year mortality than controls(106). This has lead to guidelines which recommend that LTOT for at least 15 hours per day should be offered to stable COPD patients with PaO2 < 7.3 kPa, or 7.3-8 kPa with secondary polycythaemia, peripheral oedema or pulmonary hypertension(28). However, there is uncertainty whether LTOT confers other benefits. There are conflicting data whether LTOT provision is associated with better or worse health related quality of life(107-109). While there is evidence that administration of ambulatory oxygen during laboratory based exercise improves exercise performance and reduces the severity of breathlessness at the end of exercise(112-114), it is unclear whether LTOT affects exercise capacity or free living physical activity: while it is possible that increased oxygen delivery to the peripheral muscles will enable more physical activity while using the LTOT, it is also possible that being attached to the concentrator tubing for the majority of the day will restrict physical activity. Reduced self reported independence in activities of daily living and objectively measured physical activity has been reported in LTOT patients compared to those not receiving LTOT(110, 111).

In this retrospective cohort study, our primary aim was to investigate if there were differences in physical activity levels between patients receiving LTOT and those who had been assessed

for LTOT but were found to be above criteria to receive it. Our secondary aims were to assess the levels of daily physical activity in all the patients who had been assessed for LTOT (reflecting a more severe and frail patient group) in comparison with a less severe patient group and to investigate relationships with lung physiology, peripheral muscle strength and health status.

7.2 Methods

Recruitment for this study was September 2007 to October 2008. Stable COPD patients in the LTOT assessed group were recruited from a nurse run dedicated oxygen clinic at University Hospital Aintree and were either established on LTOT or had been assessed for LTOT but were found to be above criteria. Patients had initially been referred to this clinic by a respiratory physician following a hospital admission or clinic attendance when their oxygen saturations had been recorded at a level below 90% on room air on at least one occasion. Patients were deemed suitable for LTOT if they were on optimal pharmacological treatment with PaO2 on room air < 7.3 kPa, or 7.3-8 kPa with secondary polycythaemia, peripheral oedema or pulmonary hypertension(28). The oxygen flow rate was then set at a rate aiming to achieve PaO2 > 8kPa. Patients included in this study had a diagnosis of COPD confirmed by a respiratory physician with confirmatory spirometry (post bronchodilator FEV_1 < 80% predicted and FEV_1/FVC ratio <70%). LTOT patients had been established on a stable oxygen flow rate for at least 3 months. Exclusions were a significant respiratory disease other than COPD, unstable cardiac or rheumatological disease or significant disease other than COPD which would significantly affect mobility or daily activity, cognitive impairment or COPD exacerbation (requiring oral corticosteroids, antibiotics or both) in the 4 weeks prior to

the assessment. The less severe COPD patients were those who were studied in Chapter 6: stable COPD patients who were about to commence a course of pulmonary rehabilitation. Participating subjects gave oral and written consent. The study was approved by South Sefton Ethics Committee.

Assessments

If patients agreed to take part in the study, transportation from the patient's home to the Respiratory Laboratory at University Hospital Aintree (where the assessments were carried out) was provided. A proforma was completed detailing co morbidities, medication, smoking status and social history, vaccinations and exacerbation status (recalled number of prednisolone, antibiotic courses and hospitalizations in the previous 12 months). Additionally, arterial blood gas measurements were recorded as well as the oxygen flow rate for LTOT patients. Measures of height, weight and bioimpedance were made. From the impedance, estimates of fat free mass (FFM) were calculated using a disease-specific equation(180) Measurements of post bronchodilator spirometry (FEV_1, FVC), slow vital capacity, inspiratory capacity (IC), total lung capacity (TLC), residual volume (RV) and gas transfer (TLCO and KCO) were recorded. Quadriceps force (QF) and 6 minute walk distance (6MW) were assessed. If the patient usually used ambulatory oxygen, then this was delivered during the 6MW at the patient's usual rate. Subjects completed St George's Respiratory Questionnaire (SGRQ), MRC dyspnoea scale, hospital anxiety and depression score (HAD), London Chest Activities of Daily Living Score (LCADL) and Nottingham Extended Activities of Daily Living Questionnaire (NEADL). Subjects were then asked to wear the Actiwatch (AW) or DynaPort (DP) or both monitors for 3 full consecutive days at home. When there were failed readings, the patient was requested to wear the monitor again. Physical activity levels were reflected as a composite score which was valid from either

activity monitor (as described in Chapter 2). Where data from both AW and DP were available, the DP readings were selected.

Statistical Analysis

Statistical analysis was carried out using SPSS (15.0). Variables were tested for skewness and Normality using the Shapiro-Wilks test. Variables which were not Normally distributed were logarithmically transformed and the Shapiro-Wilks test was repeated to assess Normality. Mean (sd) values were calculated and non-Normally distributed variables were expressed as median (interquartile range). Unpaired data were analysed by the independent samples t-test or Mann-Whitney U test (non parametric variables). A Spearman's correlation test was performed to assess relationships between non parametric variables. A level of significance was set at 0.01 for correlation analysis to account for multiple testing, but was set at 0.05 for all other statistical tests.

7.3 Results

35 patients agreed to take part in the LTOT assessment arm of the study, of whom 18 were receiving LTOT (LTOT) and 17 were not receiving LTOT (nonLTOT). 3 patients (2 LTOT, 1 nonLTOT) subsequently withdrew consent before the assessments were carried out and one patient (LTOT) sadly died after the assessment but before wearing the activity monitor. Full assessments were therefore carried out on 31 patients: 15 LTOT (9 male, 6 female) and 16 nonLTOT (8 male, 8 female). 11 patients wore the DynaPort only, 18 patients wore the Actiwatch only and 2 patients wore both monitors simultaneously. 5 DP readings failed initially (incorrect set up, premature device switch off or displacement of a lead or the waist

belt); 3 patients agreed to wear the monitor again and managed a successful reading. 2 subjects declined a repeat DP measurement; however, in these 2 subjects, the limb lead only had displaced at the initial reading, allowing limited data to be analysed (% time active). There were no failed AW readings. 37 patients (18 male, 19 female) were studied in the pre PR group (described in Chapter 6).

Pharmacotherapy

Of the 31 patients in the LTOT assessed group, 27 were on triple inhaled therapy (long acting beta agonist [LABA] + corticosteroid [ICS] + long acting antimuscarinic [LAMA]), 3 were receiving only LABA + ICS and 1 subject was on LABA only. Of the 15 patients receiving LTOT, 13 were on triple therapy and 2 were on only LABA + ICS. Of the 37 patients in the pre-PR group, 29 were on triple therapy, 5 were on LABA + ICS, 1 on LAMA + ICS and 2 patients were receiving ICS only. All subjects also used a prn short acting beta agonist.

Assessment for Normality and Skewdness

All data were Normally distributed with the exception of BMI, QF, $SGRQ_{SYMPTOMS}$, $SGRQ_{ACTIVITY}$, MRC, % time active and % time in intense activity. After logarithmic transformation, these variables were Normally distributed with the exception of QF, $SGRQ_{SYMPTOMS}$, $SGRQ_{ACTIVITY}$ and MRC.

7.3.1 Comparison of LTOT assessed patients with stable subjects about to start pulmonary rehabilitation

FVC % predicted, TLCO, TLCO % predicted and % time in intense activity were significantly lower in the LTOT assessed group. There was a trend towards worse FEV_1, quadriceps force, MRC score, LCADL and % time active in the LTOT assessed group but

this did not reach statistical significance. SGRQ scores, particularly the symptom and activity domains, were very high, but there were no significant differences between the 2 groups. There was also a trend towards more courses of prednisolone, antibiotics and hospitalizations in the preceding 12 months in the LTOT group, which did not reach statistical significance (Table 7.1).

Table 7.1: Comparison of LTOT assessed and pre pulmonary rehabilitation patients

Mean (sd)	LTOT assessed (n=31)	Pre PR (n=37)	p value
Age (yrs)	69.6 (10.3)	67.7 (9.6)	NS
Antibiotic courses past 12 mths	4.8 (4.2)	4.4 (4.7)	NS
Prednisolone courses past 12 mths	4.3 (4.5)	3.7 (5.0)	NS
Hospitalizations past 12 mths	1.6 (1.7)	0.9 (1.1)	NS
FEV_1 (l)	0.9 (0.3)	1.1 (0.4)	NS
FEV_1 % predicted	41.0 (12.3)	46.9 (16.0)	NS
FVC (l)	2.1 (0.7)	2.4 (0.7)	NS
FVC % predicted	71.6 (17.7)	80.8 (16.4)	<0.05
IC (l)	1.6 (0.5)	1.7 (0.5)	NS
IC (% predicted)	64.3 (18.3)	68.0 (16.4)	NS
TLCO (mmol/kPa/min)	2.8 (1.3)	3.6 (1.5)	<0.05
TLCO % predicted	34.5 (11.5)	47.3 (18.0)	<0.05
RV (l)	3.8 (1.3)	3.5 (1.4)	NS
RV % predicted	169 (66)	158 (62)	NS
RV/TLC ratio (%)	59.1 (12.3)	56.1 (9.5)	NS
BMI*	26.7 [24.1-30.8]	26.5 [22.7-28.8]	NS
FFM (kg)	49.7 (12.3)	46.3 (8.3)	NS
Hb (g/dL)	14.0 (1.8)	14.2 (1.5)	NS
QF (kg)*	21.0 [13.8-31.6]	25.8 [20.5-29.7]	NS
$SGRQ_{SYMPTOMS}$*	76.6 [65.6-86.4]	76.8 [61.6-85.2]	NS
$SGRQ_{ACTIVITY}$*	92.5 [79.7-92.5]	85.9 [76.0-92.5]	NS
$SGRQ_{IMPACT}$	51.5 (17.4)	53.2 (18.1)	NS
$SGRQ_{TOTAL}$	65.9 (12.9)	65.6 (14.4)	NS
MRC*	5 [4-5]	4 [4-5]	NS
HADa	7.3 (4.4)	8.5 (4.8)	NS
HADd	7.8 (3.8)	8.2 (3.2)	NS
London Chest ADL	41.1 (16.2)	34.5 (11.6)	NS
Nottingham Extended ADL	13.1 (3.9)	13.4 (5.0)	NS
% time active *	7.7 [5.0-11.2]	9.8 [5.6-15.0]	NS
% time in intense activity*	1.6 [0.9-2.7]	3.7 [1.9-5.8]	<0.05

*Median [interquartile range] (not Normally distributed)

7.3.2 Relationships of physical activity with other measured variables

In this patient group (31 LTOT assessed, 37 pre PR patients), objectively measured physical activity did not correlate with quadriceps force, BMI, SGRQ, HAD, LCADL or NEADL. However, there were significant correlations of % time active with age, FEV_1 % predicted and IC % predicted and % time in intense activity with FEV_1, FEV_1 % predicted, IC % predicted, RV, TLCO and TLCO % predicted (Table 7.2). However, as scatterplots 7.1-7.5 illustrate, there was much variation, so even the strongest correlations are moderate at best.

Table 7.2: Correlations of variables with physical activity (log % time active and in intense activity) in LTOT assessed and pre PR patients collectively

	Age	FEV_1	FEV_1 % predicted	IC % predicted	RV	TLCO	TLCO % predicted
Log % time active	**r= -0.33** **p<0.01**	r= 0.21 NS	**r= 0.38** **p<0.01**	**r= 0.43** **p<0.01**	r= -0.30 NS	r= 0.21 NS	r= 0.31 NS
Log % time intense activity	r= -0.27 NS	**r= 0.38** **p<0.01**	**r= 0.43** **p<0.01**	**r= 0.47** **p<0.01**	**r= -0.39** **p<0.01**	**r= 0.37** **p<0.01**	**r= 0.44** **p<0.01**

Multivariate analysis was then carried out, with age, FEV_1, FEV_1 % predicted, IC % predicted, RV, TLCO, TLCO % predicted, log BMI, log QF, $SGRQ_{TOTAL}$, LCADL, log MRC, HADa and HADd and LCADL, as dependents. Using backward multiple linear regression, none of these variables was an independent predictor of either log % time active or log % time in intense activity.

Figure 7.1: Relationship between FEV_1 and log % time active in all patients

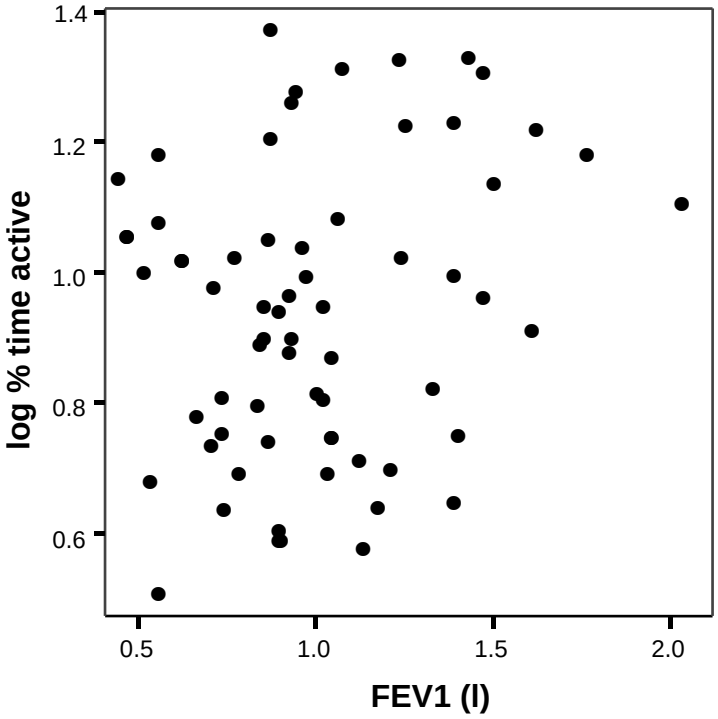


Figure 7.2: Relationship between FEV_1 and log % time in intense activity in all patients

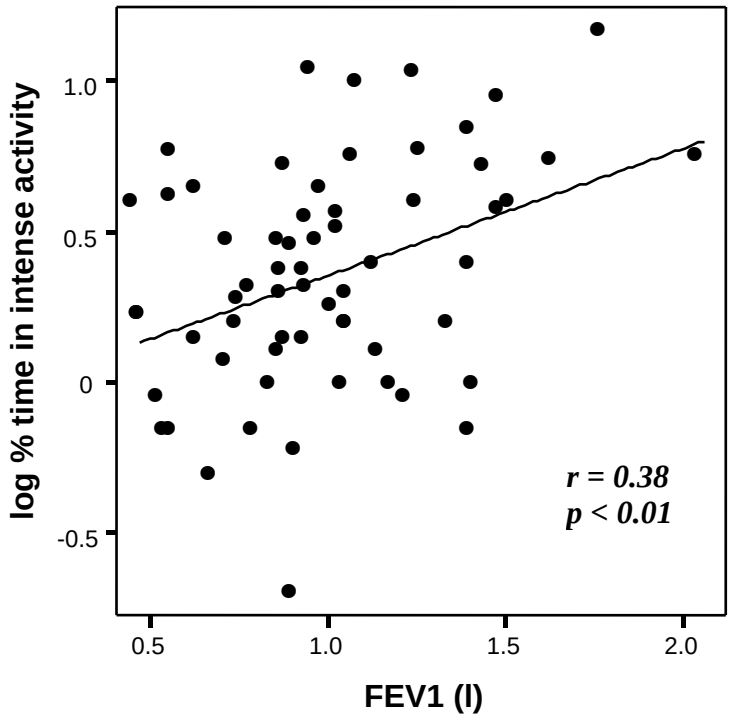


Figure 7.3: Relationship between FEV_1 % predicted and log % time active in all patients

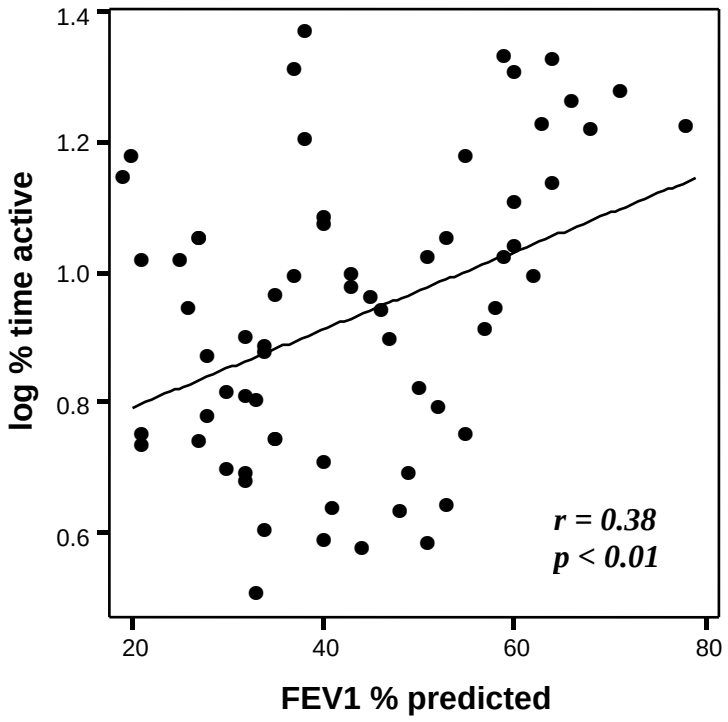


Figure 7.4: Relationship between IC % predicted and log % time in intense activity in all patients

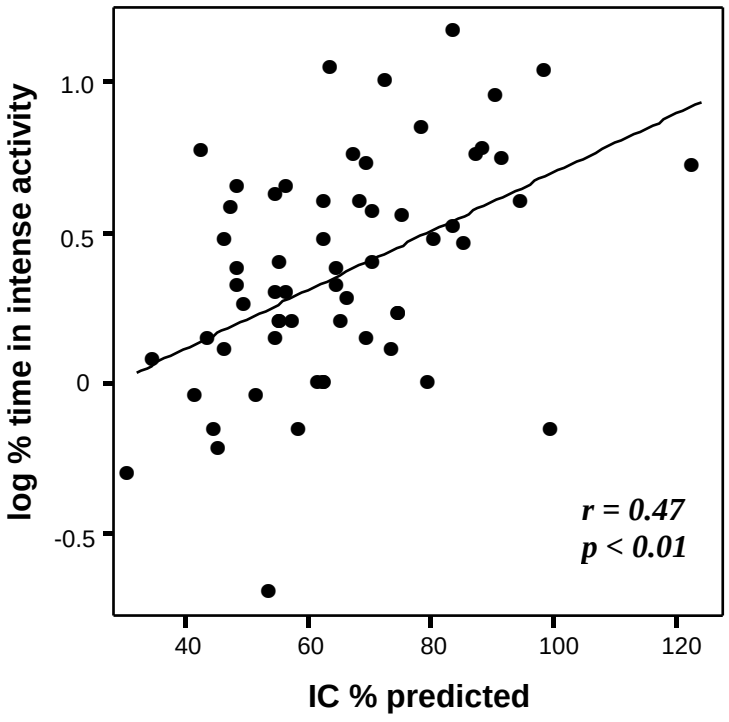
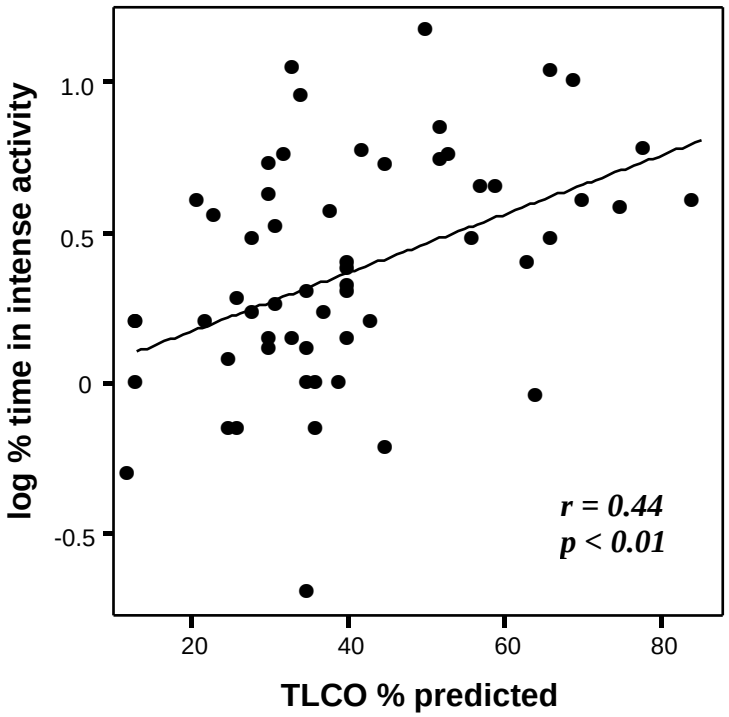


Figure 7.5: Relationship between TLCO % predicted and log % time intense activity in all patients



7.3.3 Comparison of LTOT and nonLTOT patients

Table 7.3 compares the LTOT and nonLTOT patients. As expected, the patients receiving LTOT were significantly more hypoxaemic on room air than those who were not. FEV_1 absolute but not % predicted was lower in the LTOT group, but FVC and gas transfer were comparable. Otherwise, there were no significant differences between the patient groups in terms of quadriceps force, 6 minute walk distance, SGRQ and its domains, HAD anxiety and depression scores, London Chest and Nottingham ADL scores, % time active or % time in intense activity. Although the LTOT patients had a median MRC score of 5 in comparison to a median score of 4 in the LTOT group, the difference was not statistically significant.

Table 7.3: Comparison of LTOT and nonLTOT patients

Mean (sd)	LTOT(n=15)	nonLTOT(n=16)	p value
Age (yrs)	67.3 (11.3)	71.8 (9.0)	NS
p02 room air (kPa)	6.7 (0.5)	9.0 (1.7)	<0.01
FEV_1 (l)	0.89 (0.3)	0.99 (0.3)	NS
FEV_1 % predicted	36.2 (10.5)	45.4 (12.5)	<0.05
FVC (l)	2.1 (0.8)	2.1 (0.7)	NS
FVC % predicted	67.5 (15.1)	75.4 (19.5)	NS
TLCO (mmol/kPa/min)	2.8 (1.65)	2.7 (0.7)	NS
TLCO % predicted	33.3 (14.2)	35.8 (8.1)	NS
BMI*	26.9 [24.1-37.2]	26.5 [22.6-29.7]	NS
FFM (kg)	54.2 (14.6)	45.8 (8.7)	NS
Hb (g/dL)	14.5 (1.4)	13.5 (2.0)	NS
QF (kg)	25.3 [19.3-32.2]	17.4 [12.3-31.0]	NS
QF/BMI % ratio	91.6 (35.5)	81.5 (49.9)	NS
6 minute walk (m)	215 (92)	175 (89)	NS
$SGRQ_{SYMPTOMS}$*	78.1 [69.2-86.4]	75.7 [63.1-87.8]	NS
$SGRQ_{ACTIVITY}$*	92.5 [73.0-92.5]	85.9 [80.0-92.5]	NS
$SGRQ_{IMPACT}$	51.5 (21.2)	51.5 (13.6)	NS
$SGRQ_{TOTAL}$	66.5 (15.7)	65.4 (10.0)	NS
MRC*	5 [4-5]	4 [4-5]	NS
HADa	7.2 (4.8)	7.4 (4.2)	NS
HADd	7.5 (3.9)	8.1 (3.7)	NS
London Chest ADL	43.9 (14.7)	38.6 (17.5)	NS
Nottingham Extended ADL	13.1 (3.8)	13.1 (4.2)	NS
BODE	6.8 (1.7)	6.6 (1.7)	NS
% time active *	7.9 [5.5-11.3]	7.6 [4.1-11.0]	NS
% time in intense activity*	1.6 [0.9-2.9]	1.4 [0.9-2.6]	NS

*Median [interquartile range] (not Normally distributed)

7.4 Discussion

These data suggest that a group of COPD patients who have been referred for assessment for LTOT, spent less time in intense activity (walking or more intense activity) than a milder patient group. There were moderate univariate relationships between % time active and age, between % time in intense activity and FEV_1, RV, TLCO and TLCO % predicted, and between both modalities of physical activity and FEV_1 % predicted and IC % predicted; however none of these variables independently predicted physical activity. Among patients who had been assessed for LTOT, those who met LTOT criteria and subsequently received it

showed comparable levels of physical activity to those who did not: the two patient groups were comparable with the exception of a lower FEV_1 % predicted in the LTOT group. Although clinical experience would associate LTOT assessed patients as a sicker and more frail group than patients about to commence PR, in this study they are only distinguishable from one another in certain aspects of lung physiology (FVC % predicted and gas transfer absolute and % predicted) and objective physical activity (% time in intense activity). Surprisingly, they are equivalent in terms of age, FEV_1, health status and self reported breathlessness, anxiety, depression and self reported ability to carry out daily physical activities. There were no significant differences in exacerbation or hospitalization rates in the previous 12 months between the two groups, which is surprising since a number of subjects would have been referred for LTOT assessments following exacerbations and hospitalization, while stability of disease at least over the preceding 4 weeks was a prerequisite for enrolment into PR. Unfortunately, we could not compare exercise capacity or BODE score since different field tests were used in the two groups. However, there was a difference between the groups in objectively measured intense physical activity. This suggests that physical activity monitoring, particularly measures of intense activity such as walking, may add additional information to that captured by more conventional tests. It is surprising to see that health status (as measured by SGRQ) is as poor in the LTOT assessed group as it is in the pre PR group. However, as discussed in the Chapter 6, our pre-PR patients had a much worse health status than subjects assessed in other studies. This may be the "Liverpool" effect in that the COPD patients that have participated in our different studies appear to have come from a particularly sick and static population.

Walker, evaluating COPD subjects undertaking PR, reported that FEV_1 was the strongest predictor of physical activity, as reflected in Actiwatch activity count (r=0.57) and % time mobile (r=0.51)(166). While we have found a correlation of FEV_1 with intense activity, this

is not as strong as Walker's correlation. We also found moderate correlations of physical activity with other measures of lung physiology, with the strongest correlation between IC % predicted and intense activity, but this only explained 22% of the variance.

Our data suggest that COPD patients who use LTOT have comparable levels of exercise capacity, health status, self reported breathlessness, anxiety, depression, self reported activity and actual physical activity to a similar group of patients with a higher FEV_1 % predicted who are above the criteria for LTOT. This was not a randomised controlled study, rather a retrospective assessment after the patient had been assessed for LTOT. Therefore, it is not possible to confirm cause and effect. It is possible that the LTOT patients are comparable to the non-LTOT group only because they receive LTOT. It may be the case that our patients would have worse breathlessness, exercise capacity, health status or physical activity levels if they were not receiving LTOT. The only way of establishing this would be to carry out the assessments before and after starting LTOT. However, we have shown that the use of LTOT does not appear to negatively influence physical activity: patients who are connected to oxygen tubing in the home for at least 16 hours per day show comparable levels of physical activity to patients who are not. Although measuring different outcomes, our findings mirror a different endpoint finding in Anthonisen's comparison of the NOTT and IPPB trial, where hypoxic patients treated with LTOT had comparable mortality to patients without hypoxaemia.

This study confirms the observations by ourselves and others of the sedentary lifestyle that COPD patients lead. Although the 'milder' (pre PR) COPD patients demonstrate very low levels of physical activity, spending a median of 3.7% of the waking day in intense activity such as walking, this is still better than the 1.6% of time that the LTOT assessed patients spend doing this sort of activity. Clinical experience and the natural history of COPD suggest that milder patients (similar to the pre-PR group) will progress to a more severe group

(similar to the LTOT assessed group) with time. As COPD progresses, it is also common to see decline in FEV_1 and health status with time. However, assuming that the differences between the pre PR and LTOT assessed patients reflect COPD disease progression, we have seen a decline in intense physical activity without decline in FEV_1 or health status. It is possible, therefore, that decline in physical activity is an earlier marker of disease progression than more conventional measures, although clearly this requires further investigation by means of a longitudinal follow up study.

The overall theme appears to be that both the pre PR and LTOT assessed patient groups have a poor health status and low levels of physical activity. It appears that these patients carry out just enough physical activity to try to fulfil essential daily activities. In light of the 3.7% and 1.6% of the time spent in moderate intensity activity such as walking in the pre PR and LTOT assessed patients (which equates to 27 and 12 minutes of a 12 hour waking day respectively), it is unlikely that these patients are doing much, if any walking outside of the house, and certainly unlikely that they are intending to carry out moderate intensity activity as a means of health improvement. This is supported by the minute by minute analysis of the individual readings of the DP and AW, which reveals that most periods of intense activity consist of short bursts of walking and intense physical activity with a duration of no more than 2 minutes in the majority of patients.

We have demonstrated a very poor health status in all the patient groups, particularly in the activity domain of SGRQ. Janssens reported a poor health status in 79 patients who were receiving LTOT, the majority of whom had COPD(229). However, the health status (mean $SGRQ_{TOTAL}$ 59) was better than our LTOT, nonLTOT and pre PR patient groups, and subjects walked a mean daily distance of 1.2km as measured by pedometer, which probably reflects more physical activity than the 12 minutes per day in moderate intensity activity that our LTOT patients managed. As discussed in previous chapters, we appear to have studied a

'bottomed out' COPD population who do very little physical activity in daily life. This raises the question whether we are intervening too late with our patients. As discussed in Chapter 6, although it appears that PR may have been offered to some of the patients we have studied at a worse stage of breathlessness (median MRC score 4) than guideline recommendations(209), it may be the case that PR, and possibly even pharmacotherapy, needs to be offered at an earlier stage of the disease than currently recommended.

Limitations of this study are the small numbers in each arm when comparing LTOT with non LTOT and the fact that this is a retrospective study, meaning that causality cannot be determined, as discussed earlier. We were unable to objectively measure compliance with usage in the LTOT group, although all 15 patients reported that they used the LTOT for at least 16 hours per day. Some clinicians include nocturnal oxygen saturation monitoring as part of the assessment that the LTOT was set at an adequate flow rate (based on findings in some studies of inadequate correction of nocturnal oxygen saturations in up to 48% of patients(230, 231)). This is not usual practice at our unit and was therefore not done in these patients. It is therefore possible that our LTOT patients may not have all been adequately treated with LTOT. We acknowledge that we did not correct for haemoglobin in our gas transfer analysis, which will have resulted in inaccuracies for anaemic and polycythaemic patients.

While the benefits of LTOT in reducing mortality in hypoxaemic COPD patients is established(105, 106), it is not clear whether other benefits are conferred. Reduced hospitalisations have been reported in hypoxaemic COPD patients after commencing LTOT(232, 233), although the MRC study did not demonstrate this(106). Okubadejo found that health status did not significantly improve after LTOT was started(109), and also

reported worse SGRQ in LTOT patients than the control group both before and after starting LTOT. This contrasts with our patients, where both groups had comparable health status, but SGRQ scores in both of our patient groups were worse than Okubadejo's patients. In an ancillary study to the NOTT study, it was found that patients who received continuous oxygen therapy showed mild neuropsychologic improvement but little change in emotional status or quality of life in comparison with patients who received only nocturnal oxygen(234). In contrast, Dilworth observed improved self reported general wellbeing, mobility, breathing and sleep pattern in the majority of patients after commencing LTOT(235), while Eaton also observed improvement in health status measured by the chronic respiratory questionnaire(107). While there is evidence that administering oxygen during exercise improves exercise performance in the laboratory and reduces the severity of breathlessness at the end of exercise(112-114), this may not the case in non hypoxaemic COPD patients(236). Moreover, it is less certain whether LTOT provision will bring about improved exercise capacity, particularly if the assessment of exercise capacity is carried out when the patient is not using oxygen (only two of our patients- one LTOT, one nonLTOT- received oxygen during the 6MW test since they normally used ambulatory oxygen). It is possible that LTOT leads to improved haemodynamic efficiency by means of reduced pulmonary vasoconstriction, and increased peripheral oxygen delivery due to improved cardiac function and peripheral oxygen delivery, with Morrison et al reporting evidence for the latter(237). We did not find a significant difference in exercise capacity in our LTOT patients compared with nonLTOT patients. This contrasts with Sant'Anna's study, which found significantly worse 6 minute walk distance in LTOT patients than controls (283m vs 377m). However, Sant'Anna's patients were younger with better health status and exercise capacity but worse spirometry than our subjects(108).

There are limited data on whether oxygen provision (either LTOT or ambulatory oxygen) is related to free living physical activity. Okubadejo reported worse self reported ADL's in 23 patients who were receiving LTOT compared with 19 nonLTOT controls(110). We did not find this with the same (NEADL) questionnaire. Sandland reported no increase in physical activity as measured with a uniaxial accelerometer worn on the waist in a randomized control trial of ambulatory oxygen versus air in 20 COPD patients(116). Sandland used the same accelerometer to demonstrate significantly lower activity counts in 9 patients who received LTOT than 20 patients who did not(111). However, this study was conducted on patients from a pulmonary rehabilitation register, and it is not clear from the study protocol whether readings were taken before, during or after PR, and whether this was controlled between groups. Lewis found no change in physical activity levels measured by the SenseWear armband in 10 COPD patients after commencing LTOT, although they did find an increase in heart rate variability(238).

In summary, we have demonstrated lower levels of intense physical activity in subjects who have been assessed for LTOT than a milder COPD patient group. Of the patients assessed for LTOT, those who receive it have lower FEV_1 % predicted than those who do not, but comparable health status, exercise capacity and physical activity (measured subjectively and objectively). Although we have not demonstrated additional benefits associated with LTOT, we have shown that LTOT provision is not associated with reduced levels of physical activity in daily life.

Chapter 8: Conclusions

We have studied physical activity levels in COPD patients in 3 clinical situations using 2 different types of accelerometer. Although the DynaPort recorded whole body activity and provided more comprehensive information than the Actiwatch which detected lower limb activity, there was a high failure rate with the DynaPort and, more importantly, patients did not like wearing it. By calibrating the Actiwatch (a much simpler, cheaper and lighter device) against the DynaPort, we have been able to determine thresholds of leg activity reported by the Actiwatch which reflect % time active (including low level activity such as standing) and % time in intense activity (reflecting activity such as walking), allowing us to measure surrogates of the same property using either the DynaPort or the Actiwatch.

We have demonstrated that levels of physical activity are very low in COPD subjects even when they are stable. This is despite the fact that we have investigated a relatively motivated group of individuals who were willing to take part in these studies. It may be the case that the wider COPD community as a whole has even lower levels of physical activity. Where physical activity does take place, much of it appears to be in sporadic bursts for a couple of minutes at a time. This probably reflects activity within the house such as transferring from room to room carrying out the most basic essential daily activities. Even though the stable COPD patients appear to be approaching the WHO recommendation that people undertake at least 30 minutes of moderate physical aerobic activity per day for 5 days in a week(4), they are probably not getting the health benefits that continuous sessions of moderate exercise of 10 minutes or more would achieve. Additionally, it is recommended that the target of 30 minutes' moderate physical activity be in addition to routine light intensity activities of daily living, such as self care, cooking or shopping(239).

We have demonstrated that COPD patients in the early stages of recovery after hospitalisation for exacerbation have lower levels of physical activity than stable patients, but patients who receive an early discharge home are more active than those who remain in hospital. We have shown that, while physical activity levels correlate with FEV_1 and quadriceps strength in the exacerbators, this is not the case with stable patients, and there is no correlation of physical activity with self reported breathlessness, health related quality of life or self reported physical activity limitation in either stable patients or exacerbators. This suggests that, what COPD patients actually do correlates at best only weakly with what they can do (depending on the clinical situation), and not at all with what they say they can do. Measuring actual physical activity with accelerometers provides complementary information to that obtained from questionnaires and timed walking tests.

We have shown an improvement in both exercise capacity and physical activity in the 5 weeks following the initial hospitalisation. However, these subsequently decline in the following 10 weeks to levels which are comparable to the early stages of the initial exacerbation. Just under half of subjects fail to demonstrate improved physical activity from the early stages of recovery from a COPD exacerbation to assessment in a stable phase 4 months later. This may be a reflection of the fact that 80% of the patients that we studied suffered at least 1 further exacerbation and 45% were readmitted for exacerbation in the following 4 months.

Levels of physical activity in the early stages of recovery from exacerbation predict re exacerbation and readmission in the subsequent 4 months: % time in intense activity predicts re exacerbation and % time active predicts both re exacerbation and readmission. However, baseline physical activity in this patient group does not predict mortality or readmission at 12 months.

There is emerging evidence that early outpatient pulmonary rehabilitation after exacerbation may improve health status and also reduce hospital admissions and mortality in the short term(196, 197, 204). However, it is not clear whether all COPD patients, particularly the frail group that we have studied, would benefit from this. It is also not known whether PR delivered in a different way, such as in the early stages of the exacerbation in the inpatient setting, will bring about benefit. Further studies are required to investigate this, and also whether activity monitoring may be a useful way of identifying those patients that would benefit the most from such an intervention.

We have added to previous evidence that, among stable patients who complete a course of Pulmonary Rehabilitation, there are significant improvements in levels of physical activity (% time active and % time walking) and we suggest that activity monitors that measure lower limb activity are necessary to detect this change. Our patients also demonstrate significant improvements in peripheral muscle strength, exercise capacity and depression scores after PR, and most of these changes appear to be independent of changes in physical activity. However, the improvements in depression scores and physical activity levels are lost 6 months after completion of the PR course. In this patient group, health related quality of life and self reported ability to carry out activities of daily living fail to improve after PR, and subsequently deteriorate further 6 months later. The decline in health status, depression scores and physical activity levels 6 months after PR is seen much earlier in our patients than has been reported in other studies. Our patients had a very poor health status at baseline and it may be that this is a static patient group in whom the benefits that are usually seen after PR are either not seen or are short lived. Our findings of preserved peripheral muscle strength and, to a lesser extent, exercise capacity 6 months after PR raises the possibility that while some of the physiological benefits of PR might

persist, this has not translated into a sustained change in patient behaviour. It may be the change in behaviour as reflected in sustained increases in physical activity that is necessary to result in sustained improvements in health status. Therefore, embedding long term behaviour change may be necessary if real long term benefits of PR are to be seen and sustained. While there is some evidence that prolonged or maintenance PR might confer more sustained improvements in exercise capacity, health status, self reported disability and healthcare utilisation(129, 130, 211, 219), there is also some evidence that this is not the case(132, 225). Moreover, there is a lack of data to suggest that any benefits include sustained levels of physical activity. Further research is needed in this area, to clarify whether prolonged, staggered or maintenance PR confers longer term health benefits, and whether the increased resources of implementing such measures would be cost effective.

We have demonstrated lower levels of intense activity (but not % time active) in COPD patients who have been assessed for long term oxygen therapy compared with stable patients who have a better FVC % predicted and gas diffusion capacity. There were univariate (but not multivariate) correlations between physical activity and lung physiology, but no correlation of physical activity with health status, anxiety, depression or self reported activity limitation. We have also demonstrated that COPD patients who are prescribed LTOT have comparable levels of physical activity (self reported and accelerometer measured), exercise capacity, health status, self reported breathlessness, anxiety and depression to a similar group of patients with a higher FEV_1 % predicted who are above the criteria for LTOT. We do not know whether the provision of LTOT allows hypoxaemic COPD patients to maintain levels of activity that would otherwise be worse. However, our data do at least offer some reassurance that LTOT provision is not associated with deterioration in physical activity, exercise capacity, health status, anxiety, depression or

breathlessness. The evidence for benefit of LTOT beyond mortality improvement is limited and conflicting. The only way of establishing whether LTOT leads to changes in physical activity or health status would be to carry out a large randomised control study, but the ethical implications mean this is unlikely to take place,

Across these 3 patient groups, we appear to have studied a fairly static and 'flat' COPD population who do very little physical activity in daily life and show only transient improvements after pulmonary rehabilitation or when they recover from an exacerbation. It may be the case that PR has been offered too late to some of our patients (particularly those with MRC scores 4 and 5) to gain the most benefit.

Although there are a number of complex and elaborate activity monitors available, a simple accelerometer that can detect lower limb activity (such as the Actiwatch) may be all that is required to detect physical activity in COPD patients and track changes after an intervention, exacerbation or with the progression of time. Measuring physical activity with accelerometers provides additional information about COPD patients to that provided by more conventional measures, and our data from the PR and LTOT patients suggest that a decline in objectively measured physical activity may be a more sensitive marker of disease progression than $FEV_{1.}$

Physical activity monitoring is a relatively new field and there remain many unanswered questions. Since there is a variety of different monitors which produce different outputs, the clinical relevance of these outputs is yet to be determined and there is currently no standardised measure of physical activity in COPD patients. We have reported outputs in terms of time active and time in intense activity and can compare these figures with the WHO recommendation that people undertake at least 30 minutes of moderate physical aerobic activity per day for 5 days in a

week(4), however, as discussed earlier in this chapter, 30 minutes of intermittent intense activity in carrying out essential ADL's in the home is likely to have less of a health benefit than a 30 minute intense walk. There is further uncertainty about what would constitute a clinically significant improvement or decline in physical activity following an intervention or adverse event such as an exacerbation. These are fields that require further exploration. Additionally, it should be considered whether new self reported questionnaires or other patient reported outcome measures can be developed, which incorporate patients' experiences of how COPD affects their daily lives and which better reflect actual physical activity than measures currently in use. Some of these issues may be addressed by the PROactive COPD project which is currently underway in centres across Europe.

Although the Actiwatch is better tolerated than patients than the DynaPort, it is measuring only lower limb activity. A system that records whole body activity and/or body positions that is well tolerated by the patient would be desirable and newer accelerometers such as the SenseWear and DynaPort Minimod show some promise in this regard.

Suggestions for further research

We have shown that measuring levels of physical activity in COPD patients with accelerometers does appear to offer additional information to more conventional measures in different clinical situations. However, further work is required to establish meaningful metrics that reflect prognosis and clinically significant change, and this in turn could lead to established activity levels that would act as a trigger to commence a specific intervention or a goal for patients to aim for, with the aim of improving patient outcomes.

Accelerometers could be used in COPD patients to determine:

1. Whether physical activity in the stable state predicts a patient's risk of exacerbation and hospitalisation, and whether a particular activity level can be determined that would label patients as high risk for these events.
2. Whether change in physical activity could be used to predict (and treat) the early stages of an exacerbation.
3. Which patients stand to gain most from early or inpatient pulmonary rehabilitation after hospitalisation for COPD exacerbation.
4. Which patients are more likely to benefit from high intensity, prolonged or maintenance courses of pulmonary rehabilitation.
5. Whether the provision of LTOT results in altered levels of daily physical activity.

This would allow accelerometry to evolve from a laboratory led research measure to a useful tool in clinical practice.

Publications related to the thesis

Zainudin L, **Albert P**, Ford V, Calverley P. *Are the benefits of pulmonary rehabilitation sustained after 6 months?* Eur Resp Journal 2011; Abstracts Issue P2997

Tjia-Leon E, **Albert P**, Savi D,Jack S,Calverley P. *Assessment of two physical activity monitors in COPD patients.* Eur Resp Journal 2010; Abstracts Issue P653

Abdul Hafidz MI, **Albert PS**, Walker PP, Burnett A, Calverley PMA. *Assessing diurnal variation in physical activity in COPD subjects.* AJRCCM 2010;181 Abstracts Issue: A3576

Albert PS, Hicks A, Osman Hicks V, Calverley PMA. *Early home discharge after COPD exacerbation is associated with increased physical activity.* AJRCCM 2010;181 Abstracts Issue: A2392

Ponnuswarmy A, **Albert PS**, Abdul Hafidz MI, Calverley PMA. *Can features in the early stages of recovery from COPD exacerbation predict mortality or readmission at 12 months?* AJRCCM 2010;181 Abstracts Issue: A1523

Albert PS, Abdul Hafidz MI, Ponnuswarmy A, Calverley PMA. *The relationships between reported and actual physical activity and health status in COPD patients who exacerbate.* AJRCCM 2010;181 Abstracts Issue: A1487

Albert PS, Farrar P, Ford V, Poland M, McKean S, Ward K, Calverley PMA, Davies L. *Uptake and Completion Rates in Hospital and Community Based Pulmonary Rehabilitation Programmes.* AJRCCM 2009;179 Abstracts Issue:A107

Albert PS, Jones S, Davies L, Calverley PMA. *Predictors of readmission and mortality following admission for chronic obstructive pulmonary disease exacerbation.* Thorax 2008;63 (suppl vii):A130

Albert PS, Hicks AP, Osman Hicks V, Calverley PMA. *Exercise capacity correlates with subjective questionnaires but not with actual activity in chronic obstructive pulmonary disease patients.* Thorax 2008;63 (suppl vii):A137

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Appendices

Appendix A: COPD Exacerbation Proforma

Activity Monitoring after an exacerbation of chronic obstructive pulmonary disease: the impact on daily activity at home

Patient Questionnaire

Version 1(ACT 3-Q)

Initials_____

D.O.B_____

Study Number_____

Date of Admission_____

Date of Discharge_____

Antibiotics?_____

Prednisolone?_____

Date of 1st assessment_____

Home Hospital Actrite? Y N

ASSESSMENT 1

HISTORY

Do you know what your chest condition is called? _____

Has a doctor told you that you have COPD (Chronic Obstructive Pulmonary Disease)?_____

When was it diagnosed?_____

What do you understand has caused it?_____

Do you think smoking caused your chest condition?_____

How long have you had a bad chest?_____

Have you ever been hospitalised for your chest?_____

If so, when was the last time?_____

Have you been hospitalised for your chest in the past year?_____

If so, how many times?_____

Have you taken antibiotics for your chest in the past year?_____

If so, how many times?_____

Have you taken steroids for your chest in the past year?_____

If so, how many times?_____

Have you received the 'flu vaccination in the past 12 months?_____

Have you received the pneumonia (pneumococcal) vaccination in the past 10 years?_____

ASSESSMENT 1

SMOKING HISTORY

Do you smoke? Y N Ex

When did you start?_____

When did you stop? (if you have stopped)_____

Average number cigarettes per day_____

Have you tried to give up?_____

Have you seen a smoking counsellor?_____

Have you tried Nicotine Replacement Therapy or bupropion?_____

PAST MEDICAL AND SURGICAL HISTORY

USUAL MEDICATIONS (Incl Inhalers + dose, nebs, oxygen)

SOCIAL HISTORY

Who lives at home with you?_____

Who is the main carer?_____

Type of accommodation_____
(house/bungalow/floor)

Where is the toilet situated?_____
(upstairs/downstairs/both)

Are there stairs at home?_____

Can you climb the stairs? Easily / slowly without stopping / stop once
(ring one)
stop more than once / can't climb at all / have starlift

Employment (current/previous)_____

Are you medically retired?_____

Who does: Cooking_____

Cleaning_____

Bed changing_____

Shopping_____

Can you wash yourself?_____

Can you dress yourself?_____

Do you go out socially?_____

Usually what time do you
Get out of bed?_____

Go to bed?_____

Do you have naps during the day?_____how often?_____for how long?_____

ASSESSMENT 2 : DATE_____

Since your last assessment (4 weeks ago) have you had a flare up of your chest condition requiring antibiotics and/or steroids? Details

_____
_____
_____

Since your last assessment (4 weeks ago) have there been any changes to your medications? Details

_____
_____
_____

ASSESSMENT 3 : DATE_____

Since your last assessment (8 weeks ago) have you had a flare up of your chest condition requiring antibiotics and/or steroids? Details

_____
_____
_____

Since your last assessment (8 weeks ago) have there been any changes to your medications? Details

_____
_____
_____

Appendix B: Pulmonary Rehabilitation Proforma

Activity Monitoring in COPD patients before and after Pulmonary Rehabilitation

Patient Questionnais

Version 1(ACT 1-Q)

Initials_____

D.O.B_____

Study Number_____

Date of 1st assessment_____

ASSESSMENT 1

HISTORY

Do you know what your chest condition is called? _____

Has a doctor told you that you have COPD (Chronic Obstructive Pulmonary Disease)?_____

When was it diagnosed?_____

What do you understand has caused it?_____

Do you think smoking caused your chest condition?_____

How long have you had a bad chest?_____

Have you ever been hospitalised for your chest?_____

If so, when was the last time?_____

Have you been hospitalised for your chest in the past year?_____

If so, how many times?_____

Have you taken antibiotics for your chest in the past year?_____

If so, how many times?_____

Have you taken steroids for your chest in the past year?_____

If so, how many times?_____

Have you received the 'flu vaccination in the past 12 months?_____

Have you received the pneumonia (pneumococcal) vaccination in the past 10 years?_____

ASSESSMENT 1

SMOKING HISTORY

Do you smoke? Y N Ex

When did you start?_____

When did you stop? (if you have stopped)_____

Average number cigarettes per day_____

Have you tried to give up?_____

Have you seen a smoking counsellor?_____

Have you tried Nicotine Replacement Therapy or bupropion?_____

PAST MEDICAL AND SURGICAL HISTORY

USUAL MEDICATIONS (Incl Inhalers + dose, nebs, oxygen)

SOCIAL HISTORY

Who lives at home with you?_____

Who is the main carer?_____

Type of accommodation_____
(house/bungalow/floor)

Where is the toilet situated?_____
(upstairs/downstairs/both)

Are there stairs at home?_____

Can you climb the stairs? Easily / slowly without stopping / stop once
(ring one)
stop more than once / can't climb at all / have starlift

Employment (current/previous)_____

Are you medically retired?_____

Who does: Cooking_____

Cleaning_____

Bed changing_____

Shopping_____

Can you wash yourself?_____

Can you dress yourself?_____

Do you go out socially?_____

Usually what time do you
Get out of bed?_____

Go to bed?_____

Do you have naps during the day?_____how often?_____for how long?_____

ASSESSMENT 2

STUDY NUMBER_____ **DATE_____**

Since your last assessment (4 weeks ago) have you had a flare up of your chest condition requiring antibiotics and/or steroids?
Details

_____
_____
_____

Since your last assessment (4 weeks ago) have there been any changes to your medications?
Details

_____
_____
_____

So far, have you felt any benefits from the Pulmonary Rehabilitation Programme?

-2	-1	0	1	2
Feel much worse	*Feel a little worse*	*Feel no difference*	*Feel a little improvement*	*Feel much improvement*

Comments

ASSESSMENT 3

STUDY NUMBER_____ **DATE_____**

Since your last assessment (4 weeks ago) have you had a flare up of your chest condition requiring antibiotics and/or steroids?
Details

_____
_____
_____

Since your last assessment (4 weeks ago) have there been any changes to your medications?
Details

_____
_____
_____

Have you felt any benefits from the Pulmonary Rehabilitation Programme?

-2	-1	0	1	2
Feel much worse	*Feel a little worse*	*Feel no difference*	*Feel a little improvement*	*Feel much improvement*

Comments

_____
_____
_____

ASSESSMENT 4

STUDY NUMBER_____ **DATE_____**

Since your last assessment (4 weeks ago) have you had a flare up of your chest condition requiring antibiotics and/or steroids?
Details

_____
_____
_____

Since your last assessment (4 weeks ago) have there been any changes to your medications?
Details

_____
_____
_____

Have you felt any benefits from the Pulmonary Rehabilitation Programme?

-2	-1	0	1	2
Feel much worse	*Feel a little worse*	*Feel no difference*	*Feel a little improvement*	*Feel much improvement*

Comments

_____
_____
_____

Have you been continuing any of the exercises since the programme finished?
In what way?

_____
_____
_____

ASSESSMENT 4

HISTORY

Do you know what your chest condition is called? _____

Has a doctor told you that you have COPD (Chronic Obstructive Pulmonary Disease)?_____

When was it diagnosed?_____

What do you understand has caused it?_____

Do you think smoking caused your chest condition?_____

How long have you had a bad chest?_____

Have you ever been hospitalised for your chest?_____

If so, when was the last time?_____

Have you been hospitalised for your chest in the past year?_____

If so, how many times?_____

Have you taken antibiotics for your chest in the past year?_____

If so, how many times?_____

Have you taken steroids for your chest in the past year?_____

If so, how many times?_____

Have you received the 'flu vaccination in the past 12 months?_____

Have you received the pneumonia (pneumococcal) vaccination in the past 10 years?_____

ASSESSMENT 4

SMOKING HISTORY

Do you smoke? Y N Ex

When did you start?_____

When did you stop? (if you have stopped)_____

Average number cigarettes per day_____

Have you tried to give up?_____

Have you seen a smoking counsellor?_____

Have you tried Nicotine Replacement Therapy or bupropion?_____

PAST MEDICAL AND SURGICAL HISTORY

USUAL MEDICATIONS (Incl Inhalers + dose, nebs, oxygen)

SOCIAL HISTORY

Who lives at home with you?_____

Who is the main carer?_____

Type of accommodation_____
(house/bungalow/floor)

Where is the toilet situated?_____
(upstairs/downstairs/both)

Are there stairs at home?_____

Can you climb the stairs? Easily / slowly without stopping / stop once
(ring one)
stop more than once / can't climb at all / have starlift

Employment (current/previous)_____

Are you medically retired?_____

Who does: Cooking_____

Cleaning_____

Bed changing_____

Shopping_____

Can you wash yourself?_____

Can you dress yourself?_____

Do you go out socially?_____

Usually what time do you
Get out of bed?_____

Go to bed?_____

Do you have naps during the day?_____how often?_____for how long?_____

Appendix C: LTOT Assessment Proforma

Assessing activity in chronic obstructive pulmonary disease patients assessed for long term oxygen therapy

Patient Questionnaire

Version 1(ACT 4-Q)

***Initials*_____**

***D.O.B*_____**

***Study Number*_____**

***Date of assessment*_____**

ABG Analysis (Air/O2)

Patient reported usage/day (hrs)

HISTORY

Do you know what your chest condition is called? _____

Has a doctor told you that you have COPD (Chronic Obstructive Pulmonary Disease)?_____

When was it diagnosed?_____

What do you understand has caused it?_____

Do you think smoking caused your chest condition?_____

How long have you had a bad chest?_____

Have you ever been hospitalised for your chest?_____

If so, when was the last time?_____

Have you been hospitalised for your chest in the past year?_____

If so, how many times?_____

Have you taken antibiotics for your chest in the past year?_____

If so, how many times?_____

Have you taken steroids for your chest in the past year?_____

If so, how many times?_____

Have you received the 'flu vaccination in the past 12 months?_____

Have you received the pneumonia (pneumococcal) vaccination in the past 10 years?_____

SMOKING HISTORY

Do you smoke? Y N Ex

When did you start?_____

When did you stop? (if you have stopped)_____

Average number cigarettes per day_____

Have you tried to give up?_____

Have you seen a smoking counsellor?_____

Have you tried Nicotine Replacement Therapy or bupropion?_____

PAST MEDICAL AND SURGICAL HISTORY

USUAL MEDICATIONS (Incl Inhalers + dose, nebs, oxygen)

SOCIAL HISTORY

Who lives at home with you?_____

Who is the main carer?_____

Type of accommodation_____
(house/bungalow/floor)

Where is the toilet situated?_____
(upstairs/downstairs/both)

Are there stairs at home?_____

Can you climb the stairs? Easily / slowly without stopping / stop once
(ring one)
stop more than once / can't climb at all / have starlift

Employment (current/previous)_____

Are you medically retired?_____

Who does: Cooking_____

Cleaning_____

Bed changing_____

Shopping_____

Can you wash yourself?_____

Can you dress yourself?_____

Do you go out socially?_____

Usually what time do you
Get out of bed?_____

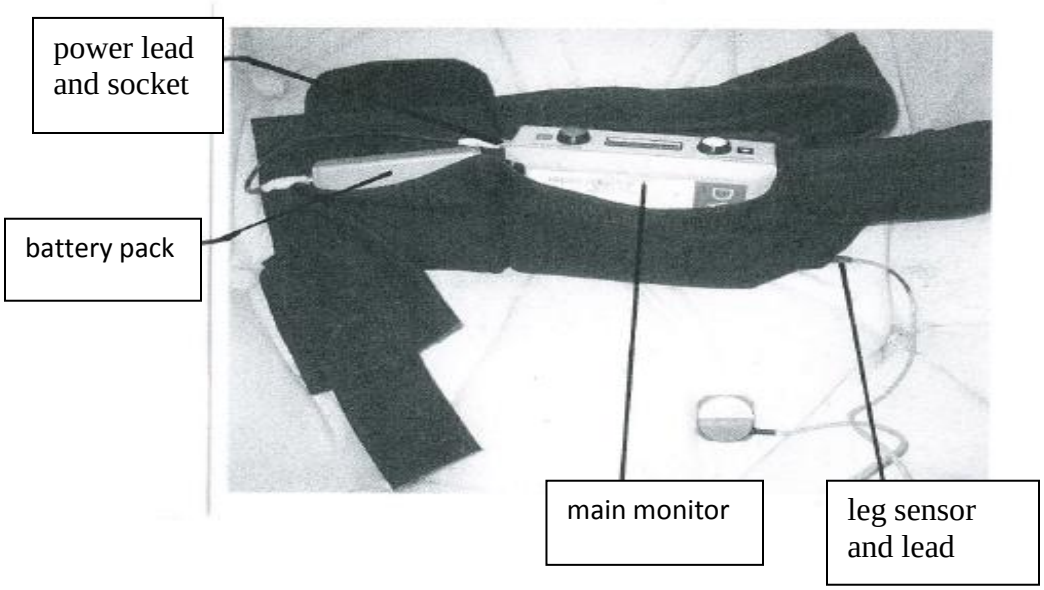
Go to bed?_____

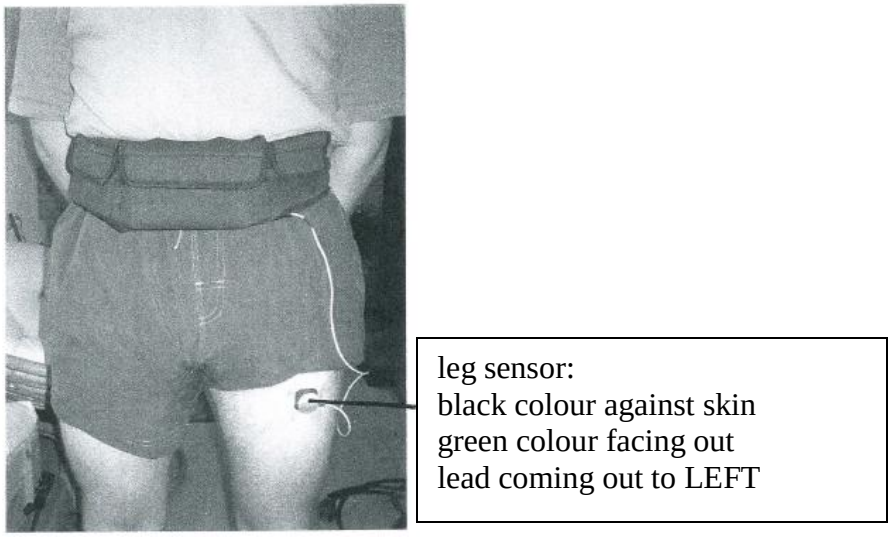
Do you have naps during the day?_____how often?_____for how long?_____

Appendix D: Instructions for using the DynaPort Activitv Monitor

Putting the monitor on

1. Place the main unit around your waist with the main monitor to the front in the middle: use the Velcro to attach the strap comfortably.
2. Tape the leg sensor to the TOP of your LEFT THIGH
3. Ensure that the BLACK colour of the leg sensor is against your SKIN,
   And the GREEN colour is FACING OUT,
   With the lead coming out to the LEFT
4. You can then put on your lower clothes on top of the leg sensor





To begin recording

1. Press the green button on the recorder. The screen will say: *"Dynaport System. Start measuring? "*
2. Press the green button again. The screen will say: *"Patient Correct? "*
3. Press the green button again. The screen will say: *"Please stand up? Ready? "*
4. Stand up and face forwards. Press the green button once more. Wait 5 seconds
5. The display should then state: *"Time: 10.53*
   Remaining: 12.29 " (or different digits)

The activity monitor is now recording. Close the pouch and continue with the rest of your day.

This may not work first time; the monitor may display "error" or "leg sensor error". Check that the leads have not become loose from the main monitor and ensure that the leg sensor is correctly positioned as described on the diagram.

SIMPLY UNDO THE STRAPS AND REMOVE THE RECORDER IF NEEDED FOR BATHROOM BREAKS- DO NOT SWITCH IT OFF. REMEMBER TO PUT IT BACK ON STRAIGHT AWAY AFTERWARDS

Ending the recording (before going to bed)

1. Simply unplug the power lead on the RIGHT of the monitor
2. Remove the equipment

Next morning (as soon as you are out of bed)- restarting the monitor

1. Change the memory card - make sure it is properly pushed in
2. Change the batteries if required (1 set of batteries should last 2 days)
3. **Plug the power lead back into the socket on the RIGHT of the monitor**
4. Follow the instructions above as for day 1
5. Use new tape to secure the leg sensor - **make sure it is correctly positioned**

At the end of the day, before going to bed, again unplug the power lead, then remove the device.

If you have any problems, call Paul Albert on 0151 529 2783 or 0772 0894790